SID 7 - free of prior art

SID 9 - free of prior art

GenCore version 4.5

OM nucleic - nucleic search, using sw model

Run on: April 5, 2001, 05:27:18 ; Search time 174.64 Seconds
(without alignments)
688.420 Million cell updates/sec

Title: US-09-380-419A-1
Perfect score: 746
Sequence: 1 acaagaatctgcattcaccc.....aagagatcatctgttgctat 746

Scoring table: IDENTITY_NUC
Gapop 10.0 , Gapext 1.0

Searched: 280836 seqs, 80580151 residues

Total number of hits satisfying chosen parameters: 561672

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : Issued_Patents_NA:*
1: /cgn2_6/ptodata/1/ina/5A_COMB.seq:*
2: /cgn2_6/ptodata/1/ina/5B_COMB.seq:*
3: /cgn2_6/ptodata/1/ina/6_COMB.seq:*
4: /cgn2_6/ptodata/1/ina/PCTUS_COMB.seq:*
5: /cgn2_6/ptodata/1/ina/backfiles1.seq:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	656	87.9	996	1	US-08-671-525B-7	Sequence 7, Appli
2	656	87.9	996	1	US-08-672-109B-7	Sequence 7, Appli
3	656	87.9	996	1	US-08-842-045-7	Sequence 7, Appli
4	656	87.9	996	2	US-08-842-238-7	Sequence 7, Appli
5	656	87.9	996	3	US-08-629-335B-7	Sequence 7, Appli
6	654.4	87.7	1671	2	US-08-662-560-1	Sequence 1, Appli
7	654.4	87.7	1671	2	US-08-780-749A-5	Sequence 5, Appli
8	649.6	87.1	1671	3	US-08-706-281A-15	Sequence 15, Appl
9	347.8	46.6	975	1	US-08-671-525B-9	Sequence 9, Appli
10	347.8	46.6	975	1	US-08-672-109B-9	Sequence 9, Appli
11	347.8	46.6	975	1	US-08-842-045-9	Sequence 9, Appli
12	347.8	46.6	975	2	US-08-842-238-9	Sequence 9, Appli

13	347.8	46.6	975	3	US-08-629-335B-9	Sequence 9, Appli
14	346.2	46.4	978	3	US-08-706-281A-17	Sequence 17, Appl
15	319.4	42.8	1080	1	US-08-671-525B-5	Sequence 5, Appli
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18	319.4	42.8	1080	2	US-08-842-238-5	Sequence 5, Appli
19	319.4	42.8	1080	3	US-08-629-335B-5	Sequence 5, Appli
20	301.8	40.5	1338	2	US-08-044-812A-3	Sequence 3, Appli
21	301.8	40.5	1338	2	US-08-475-637-3	Sequence 3, Appli
22	300.2	40.2	1338	3	US-08-706-281A-11	Sequence 11, Appl
23	255.2	34.2	1015	1	US-08-671-525B-3	Sequence 3, Appli
24	255.2	34.2	1015	1	US-08-672-109B-3	Sequence 3, Appli
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26	255.2	34.2	1015	2	US-08-842-238-3	Sequence 3, Appli
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29	255.2	34.2	2012	1	US-08-077-673-3	Sequence 3, Appli
30	255.2	34.2	2012	1	US-08-478-992-3	Sequence 3, Appli
31	255.2	34.2	2012	3	US-09-105-298-3	Sequence 3, Appli
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33	241.2	32.3	1108	1	US-07-866-560-5	Sequence 5, Appli
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35	241.2	32.3	1108	1	US-08-478-992-5	Sequence 5, Appli
36	241.2	32.3	1108	3	US-09-105-298-5	Sequence 5, Appli
37	236.4	31.7	1108	3	US-08-706-281A-9	Sequence 9, Appli
38	236	31.6	951	1	US-08-671-525B-1	Sequence 1, Appli
39	236	31.6	951	1	US-08-672-109B-1	Sequence 1, Appli
40	236	31.6	951	1	US-08-842-045-1	Sequence 1, Appli
41	236	31.6	951	2	US-08-842-238-1	Sequence 1, Appli
42	236	31.6	951	3	US-08-629-335B-1	Sequence 1, Appli
43	234.4	31.4	1633	1	US-07-866-979-5	Sequence 5, Appli
44	232.8	31.2	1633	2	US-08-466-906B-5	Sequence 5, Appli
45	232.8	31.2	1633	3	US-08-706-281A-5	Sequence 5, Appli

ALIGNMENTS

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RESULT   1
US-08-671-525B-7
; Sequence 7, Application US/08671525B
; Patent No. 5703220
;  GENERAL INFORMATION:
;    APPLICANT:  Yamada, Tadataka
;    APPLICANT:  Gantz, Ira
;    TITLE OF INVENTION:  Genes Encoding Melanocortin Receptors
;    NUMBER OF SEQUENCES:  23
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Harness, Dickey & Pierce, P.L.C.
;      STREET:  P.O. Box 828
;      CITY:  Bloomfield Hills
;      STATE:  MI
;      COUNTRY:  US
;      ZIP:  48303
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
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;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.25
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/671,525B
;       FILING DATE:  June 27, 1996
;       CLASSIFICATION:  435
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  Smith, DeAnn F.
;       REGISTRATION NUMBER:  36683
;       REFERENCE/DOCKET NUMBER:  2115-000853DVB
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (810)641-1600
;       TELEFAX:  (810)641-0270
;   INFORMATION FOR SEQ ID NO:  7:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  996 base pairs
;       TYPE:  nucleic acid
;       STRANDEDNESS:  double
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  DNA (genomic)
;     HYPOTHETICAL:  NO
;     ANTI-SENSE:  NO
;     ORIGINAL SOURCE:
;       ORGANISM:  homo sapiens
;     FEATURE:
;       NAME/KEY:  CDS
;       LOCATION:  1..996
US-08-671-525B-7
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sid 5 · 200 - 219

sid 6 : comp 947-9[illegible]

sid 8 : 477-495

[illegible] : [illegible] - 930 (comp)

Query Match 87.9%; Score 656; DB 1; Length 996;
Best Local Similarity 92.4%; Pred. No. 9.1e-178;
Matches 689; Conservative 1; Mismatches 56; Indels 0; Gaps 0;

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Qy     421 atgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccaggca 480
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Db     635 ATGTCCACATGTTCCTGATGGCCAGGCTTCACATTAAGAGGATTGCTGTCCTCCCCGGCA 694

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Db     695 CTGGTGCCATCCGCCAAGGTGCCAATATGAAGGGAGCGATTACCTTGACCATCCTGATTG 754

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Db     755 GCGTCTTTGTTGTCTGCTGGGCCCCATTCTTCCTCCACTTAATATTCTACATCTCTTGTC 814

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Qy     721 ccttcaaagagatcatctgttgctat 746
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Db     935 CCTTCAAAGAGATCATCTGTTGCTAT 960
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RESULT 2
US-08-672-109B-7
; Sequence 7, Application US/08672109B
; Patent No. 5710265
; GENERAL INFORMATION:
; APPLICANT: Yamada, Tadataka
; APPLICANT: Gantz, Ira
; TITLE OF INVENTION: Genes Encoding Melanocortin Receptors
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Harness, Dickey & Pierce, P.L.C.
; STREET: P.O. Box 828
; CITY: Bloomfield Hills
; STATE: MI
; COUNTRY: US
; ZIP: 48303
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/672,109B
; FILING DATE: June 27, 1996
; CLASSIFICATION: 536
; ATTORNEY/AGENT INFORMATION:
; NAME: Smith, DeAnn F.

; REGISTRATION NUMBER: 36683
; REFERENCE/DOCKET NUMBER: 2115-000853DVC
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (810)641-1600
; TELEFAX: (810)641-0270
; INFORMATION FOR SEQ ID NO: 7:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 996 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: double
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; ORIGINAL SOURCE:
; ORGANISM: homo sapiens
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 1..996
US-08-672-109B-7

Query Match 87.9%; Score 656; DB 1; Length 996;
Best Local Similarity 92.4%; Pred. No. 9.1e-178;
Matches 689; Conservative 1; Mismatches 56; Indels 0; Gaps 0;

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Db    515 GTATCTGGGCAGCTTGCACGGTTTCAGGCATTTTGTTCATCATTTACTCAGATAGTAGTG 574

Qy    361 ctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctctct 420
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Db    635 ATGTCCACATGTTCCTGATGGCCAGGCTTCACATTAAGAGGATTGCTGTCCTCCCCGGCA 694
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RESULT 3
US-08-842-045-7
; Sequence 7, Application US/08842045
; Patent No. 5817787
; GENERAL INFORMATION:
; APPLICANT: Yamada, Tadataka
; APPLICANT: Gantz, Ira
; TITLE OF INVENTION: Genes Encoding Melanocortin Receptors
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Harness, Dickey & Pierce, P.L.C.
; STREET: P.O. Box 828
; CITY: Bloomfield Hills
; STATE: MI
; COUNTRY: US
; ZIP: 48303
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/842,045
; FILING DATE:
; CLASSIFICATION: 536
; ATTORNEY/AGENT INFORMATION:
; NAME: Smith, DeAnn F.
; REGISTRATION NUMBER: 36683
; REFERENCE/DOCKET NUMBER: 2115-000853DVE
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (810)641-1600
; TELEFAX: (810)641-0270
; INFORMATION FOR SEQ ID NO: 7:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 996 base pairs

; TYPE: nucleic acid
; STRANDEDNESS: double
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; ORIGINAL SOURCE:
; ORGANISM: homo sapiens
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 1..996
US-08-842-045-7

Query Match 87.9%; Score 656; DB 1; Length 996;
Best Local Similarity 92.4%; Pred. No. 9.1e-178;
Matches 689; Conservative 1; Mismatches 56; Indels 0; Gaps 0;

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Qy      1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Db    215 ACAAGAATCTGCATTCACCCATGTACTTTTTCATCTGCAGCTTGGCTGTGGCTGATATGC 274

Qy     61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
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Db    275 TGGTGAGCGTTTCAAATGGATCAGAAACCATTATCATCACCCTATTAAACAGTACAGATA 334

Qy    121 cggacgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgtagct 180
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Db    335 CGGATGCACAGAGTTTCACAGTGAATATTGATAATGTCATTGACTCGGTGATCTGTAGCT 394

Qy    181 ccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttactatct 240
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Db    395 CCTTGCTTGCATCCATTTGCAGCCTGCTTTCAATTGCAGTGGACAGGTACTTTACTATCT 454

Qy    241 tttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatcagtt 300
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Db    455 TCTATGCTCTCCAGTACCATAACATTATGACAGTTAAGCGGGTTGGGATCATCATAAGTT 514

Qy    301 gtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagcagtg 360
          |||||||||||  |||||||| || ||  |||||||||||||||||||||||| ||||
Db    515 GTATCTGGGCAGCTTGCACGGTTTCAGGCATTTTGTTCATCATTTACTCAGATAGTAGTG 574

Qy    361 ctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctctct 420
          |||| || |||||||||| ||| ||||||||||||||||||||||||||||||||||||
Db    575 CTGTCATCATCTGCCTCATCACCATGTTCTTCACCATGCTGGCTCTCATGGCTTCTCTCT 634

Qy    421 atgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccaggca 480
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Db    635 ATGTCCACATGTTCCTGATGGCCAGGCTTCACATTAAGAGGATTGCTGTCCTCCCCGGCA 694

Qy    481 ctggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttgattg 540
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Db    695 CTGGTGCCATCCGCCAAGGTGCCAATATGAAGGGAGCGATTACCTTGACCATCCTGATTG 754

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Db    755 GCGTCTTTGTTGTCTGCTGGGCCCCATTCTTCCTCCACTTAATATTCTACATCTCTTGTC 814
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Db     935 CCTTCAAAGAGATCATCTGTTGCTAT 960
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RESULT   4
US-08-842-238-7
; Sequence 7, Application US/08842238
; Patent No. 5869257
;  GENERAL INFORMATION:
;    APPLICANT:  Yamada, Tadataka
;    APPLICANT:  Gantz, Ira
;    TITLE OF INVENTION:  Genes Encoding Melanocortin Receptors
;    NUMBER OF SEQUENCES:  23
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Harness, Dickey & Pierce, P.L.C.
;      STREET:  P.O. Box 828
;      CITY:  Bloomfield Hills
;      STATE:  MI
;      COUNTRY:  US
;      ZIP:  48303
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/842,238
;      FILING DATE:
;      CLASSIFICATION:  435
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Smith, DeAnn F.
;      REGISTRATION NUMBER:  36683
;      REFERENCE/DOCKET NUMBER:  2115-000853DVD
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (810)641-1600
;      TELEFAX:  (810)641-0270
;  INFORMATION FOR SEQ ID NO:  7:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  996 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  double
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  DNA (genomic)
;    HYPOTHETICAL:  NO
;    ANTI-SENSE:  NO
;    ORIGINAL SOURCE:
;      ORGANISM:  homo sapiens
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; FEATURE:
; NAME/KEY: CDS
; LOCATION: 1..996
US-08-842-238-7

Query Match 87.9%; Score 656; DB 2; Length 996;
Best Local Similarity 92.4%; Pred. No. 9.1e-178;
Matches 689; Conservative 1; Mismatches 56; Indels 0; Gaps 0;

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Qy      1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Db    215 ACAAGAATCTGCATTCACCCATGTACTTTTTCATCTGCAGCTTGGCTGTGGCTGATATGC 274

Qy     61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
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Db    275 TGGTGAGCGTTTCAAATGGATCAGAAACCATTATCATCACCCTATTAAACAGTACAGATA 334

Qy    121 cggacgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgtagct 180
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Db    335 CGGATGCACAGAGTTTCACAGTGAATATTGATAATGTCATTGACTCGGTGATCTGTAGCT 394

Qy    181 ccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttactatct 240
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Db    395 CCTTGCTTGCATCCATTTGCAGCCTGCTTTCAATTGCAGTGGACAGGTACTTTACTATCT 454

Qy    241 tttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatcagtt 300
          | |||||||||||||||||||||||||||||||||||||||||||||| |||||||| ||||
Db    455 TCTATGCTCTCCAGTACCATAACATTATGACAGTTAAGCGGGTTGGGATCATCATAAGTT 514

Qy    301 gtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagcagtg 360
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Db    515 GTATCTGGGCAGCTTGCACGGTTTCAGGCATTTTGTTCATCATTTACTCAGATAGTAGTG 574

Qy    361 ctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctctct 420
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Db    575 CTGTCATCATCTGCCTCATCACCATGTTCTTCACCATGCTGGCTCTCATGGCTTCTCTCT 634

Qy    421 atgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccaggca 480
          |||||||||||||||| |||||||| || |||||||||||||| || |||||||| ||||
Db    635 ATGTCCACATGTTCCTGATGGCCAGGCTTCACATTAAGAGGATTGCTGTCCTCCCCGGCA 694

Qy    481 ctggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttgattg 540
          ||||  |||||||||||||||||| |||||||| || |||||| |||||||| ||||||
Db    695 CTGGTGCCATCCGCCAAGGTGCCAATATGAAGGGAGCGATTACCTTGACCATCCTGATTG 754

Qy    541 gggtctttgtggtctgctgggcccccttcttcctccacttaatattctatatctcctgcc 600
          | |||||||| |||||||||||||| |||||||||||||||||||||| ||||| || |
Db    755 GCGTCTTTGTTGTCTGCTGGGCCCCATTCTTCCTCCACTTAATATTCTACATCTCTTGTC 814

Qy    601 cccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctcatcctgatca 660
          | |||||||||||  |||||||||||||||||||||||||| |||||||||| |||||||
Db    815 CTCAGAATCCATATTGTGTGTGCTTCATGTCTCACTTTAACTTGTATCTCATACTGATCA 874

Qy    661 tgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgaggaaaa 720
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Db    875 TGTGTAATTCAATCATCGATCCTCTGATTTATGCACTCCGGAGTCAAGAACTGAGGAAAA 934
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Qy     721 ccttcaaagagatcatctgttgctat 746
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Db     935 CCTTCAAAGAGATCATCTGTTGCTAT 960


RESULT   5
US-08-629-335B-7
; Sequence 7, Application US/08629335B
; Patent No. 6117975
;  GENERAL INFORMATION:
;    APPLICANT:  Yamada, Tadataka
;    APPLICANT:  Gantz, Ira
;    TITLE OF INVENTION:  Genes Encoding Melanocortin Receptors
;    NUMBER OF SEQUENCES:  23
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Harness, Dickey & Pierce, P.L.C.
;      STREET:  P.O. Box 828
;      CITY:  Bloomfield Hills
;      STATE:  MI
;      COUNTRY:  US
;      ZIP:  48303
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/629,335B
;      FILING DATE:  July 23, 1996
;      CLASSIFICATION:  435
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Smith, DeAnn F.
;      REGISTRATION NUMBER:  36683
;      REFERENCE/DOCKET NUMBER:  2115-000853DVA
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (810)641-1600
;      TELEFAX:  (810)641-0270
;  INFORMATION FOR SEQ ID NO:  7:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  996 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  double
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  DNA (genomic)
;    HYPOTHETICAL:  NO
;    ANTI-SENSE:  NO
;    ORIGINAL SOURCE:
;      ORGANISM:  homo sapiens
;    FEATURE:
;      NAME/KEY:  CDS
;      LOCATION:  1..996
US-08-629-335B-7

  Query Match             87.9%;  Score 656;  DB 3;  Length 996;
  Best Local Similarity   92.4%;  Pred. No. 9.1e-178;
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Matches 689; Conservative 1; Mismatches 56; Indels 0; Gaps 0;

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Qy       1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Db     215 ACAAGAATCTGCATTCACCCATGTACTTTTTCATCTGCAGCTTGGCTGTGGCTGATATGC 274

Qy      61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
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Db     275 TGGTGAGCGTTTCAAATGGATCAGAAACCATTATCATCACCCTATTAAACAGTACAGATA 334

Qy     121 cggacgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgtagct 180
           |||| ||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Db     335 CGGATGCACAGAGTTTCACAGTGAATATTGATAATGTCATTGACTCGGTGATCTGTAGCT 394

Qy     181 ccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttactatct 240
           |||| || || || |||||||||||||||| |||||||||||||||| ||||||||||
Db     395 CCTTGCTTGCATCCATTTGCAGCCTGCTTTCAATTGCAGTGGACAGGTACTTTACTATCT 454

Qy     241 tttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatcagtt 300
           | ||||||||||||||||||||||||||||||||||||||||||||| |||||||| ||||
Db     455 TCTATGCTCTCCAGTACCATAACATTATGACAGTTAAGCGGGTTGGGATCATCATAAGTT 514

Qy     301 gtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagcagtg 360
           |||||||||||  |||||||| || ||  |||||||||||||||||||||||| ||||
Db     515 GTATCTGGGCAGCTTGCACGGTTTCAGGCATTTTGTTCATCATTTACTCAGATAGTAGTG 574

Qy     361 ctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctctct 420
           |||| || |||||||||| ||| ||||||||||||||||||||||||||||||||||||
Db     575 CTGTCATCATCTGCCTCATCACCATGTTCTTCACCATGCTGGCTCTCATGGCTTCTCTCT 634

Qy     421 atgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccaggca 480
           |||||||||||||||| |||||||| || |||||||||||||| || |||||||| ||||
Db     635 ATGTCCACATGTTCCTGATGGCCAGGCTTCACATTAAGAGGATTGCTGTCCTCCCCGGCA 694

Qy     481 ctggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttgattg 540
           ||||  |||||||||||||||||| |||||||| || |||||| |||||||| ||||||
Db     695 CTGGTGCCATCCGCCAAGGTGCCAATATGAAGGGAGCGATTACCTTGACCATCCTGATTG 754

Qy     541 gggtctttgtggtctgctgggcccccttcttcctccacttaatattctatatctcctgcc 600
           | |||||||| |||||||||||||| |||||||||||||||||||||| ||||| || |
Db     755 GCGTCTTTGTTGTCTGCTGGGCCCCATTCTTCCTCCACTTAATATTCTACATCTCTTGTC 814

Qy     601 cccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctcatcctgatca 660
           | |||||||||||  |||||||||||||||||||||||||| ||||||||||  |||||||
Db     815 CTCAGAATCCATATTGTGTGTGCTTCATGTCTCACTTTAACTTGTATCTCATACTGATCA 874

Qy     661 tgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgaggaaaa 720
           ||||||||||  ||||||:|||| |||||||||||||||||||| ||||||||||||||||
Db     875 TGTGTAATTCAATCATCGATCCTCTGATTTATGCACTCCGGAGTCAAGAACTGAGGAAAA 934

Qy     721 ccttcaaagagatcatctgttgctat 746
           |||||||||||||||||||||||||||
Db     935 CCTTCAAAGAGATCATCTGTTGCTAT 960
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RESULT 6
US-08-662-560-1

; Sequence 1, Application US/08662560
; Patent No. 5908609
; GENERAL INFORMATION:
; APPLICANT: Lee, Frank
; APPLICANT: Huszar, Dennis
; APPLICANT: Wei, Gu
; TITLE OF INVENTION: SCREENING METHODS FOR COMPOUNDS
; TITLE OF INVENTION: USEFUL IN THE REGULATION OF BODY WEIGHT
; NUMBER OF SEQUENCES: 2
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Pennie & Edmonds
; STREET: 1155 Avenue of the Americas
; CITY: New York
; STATE: NY
; COUNTRY: USA
; ZIP: 10036/2711
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Diskette
; COMPUTER: IBM Compatible
; OPERATING SYSTEM: DOS
; SOFTWARE: FastSEQ Version 2.0
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/662,560
; FILING DATE: 10-JUN-1996
; CLASSIFICATION: 435
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER:
; FILING DATE:
; ATTORNEY/AGENT INFORMATION:
; NAME: Coruzzi, Laura A
; REGISTRATION NUMBER: 30,742
; REFERENCE/DOCKET NUMBER: 7853-060
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 212-790-9090
; TELEFAX: 212-869=8864
; TELEX: 66141 PENNIE
; INFORMATION FOR SEQ ID NO: 1:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 1671 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; FEATURE:
; NAME/KEY: Coding Sequence
; LOCATION: 394...1389
; OTHER INFORMATION:
US-08-662-560-1

SID 5 = 593 - 612

SID 6 = Comp 1340 - 1359

SID 8 = 870 - 888

SID 10 = 1353 - 1332 Comp

Query Match 87.7%; Score 654.4; DB 2; Length 1671;
Best Local Similarity 92.2%; Pred. No. 3.2e-177;
Matches 688; Conservative 1; Mismatches 57; Indels 0; Gaps 0;

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Db    608 ACAAGAATCTGCATTCACCCATGTACTTTTTCATCTGCAGCTTGGCTGTGGCTGATATGC 667
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Qy      61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
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Db     668 TGGTGAGCGTTTCAAATGGATCAGAAACCATTATCATCACCCTATTAAACAGTACAGATA 727

Qy     121 cggacgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgtagct 180
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Db     728 CGGATGCACAGAGTTTCACAGTGAATATTGATAATGTCATTGACTCGGTGATCTGTAGCT 787

Qy     181 ccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttactatct 240
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Db     788 CCTTGCTTGCATCCATTTGCAGCCTGCTTTCAATTGCAGTGGACAGGTACTTTACTATCT 847

Qy     241 tttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatcagtt 300
           |  ||||||||||||||||||||||||||||||||||||||||||||  ||||  |||  ||||
Db     848 TCTATGCTCTCCAGTACCATAACATTATGACAGTTAAGCGGGTTGGGATCAGCATAAGTT 907

Qy     301 gtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagcagtg 360
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Db     908 GTATCTGGGCAGCTTGCACGGTTTCAGGCATTTTGTTCATCATTTACTCAGATAGTAGTG 967

Qy     361 ctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctctct 420
           ||||  ||  ||||||||||  |||  ||||||||||||||||||||||||||||||||||
Db     968 CTGTCATCATCTGCCTCATCACCATGTTCTTCACCATGCTGGCTCTCATGGCTTCTCTCT 1027

Qy     421 atgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccaggca 480
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Db    1028 ATGTCCACATGTTCCTGATGGCCAGGCTTCACATTAAGAGGATTGCTGTCCTCCCCGGCA 1087

Qy     481 ctggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttgattg 540
           ||||  ||||||||||||||||||  ||||||||  ||  ||||||  ||||||||  ||||||
Db    1088 CTGGTGCCATCCGCCAAGGTGCCAATATGAAGGGAGCGATTACCTTGACCATCCTGATTG 1147

Qy     541 gggtctttgtggtctgctgggcccccttcttcctccacttaatattctatatctcctgcc 600
           |  ||||||||  ||||||||||||||  ||||||||||||||||||||||||  |||||  ||  |
Db    1148 GCGTCTTTGTTGTCTGCTGGGCCCCATTCTTCCTCCACTTAATATTCTACATCTCTTGTC 1207

Qy     601 cccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctcatcctgatca 660
           |  ||||||||||  ||||||||||||||||||||||||||  ||||||||||  |||||||
Db    1208 CTCAGAATCCATATTGTGTGTGCTTCATGTCTCACTTTAACTTGTATCTCATACTGATCA 1267

Qy     661 tgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgaggaaaa 720
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Db    1268 TGTGTAATTCAATCATCGATCCTCTGATTTATGCACTCCGGAGTCAAGAACTGAGGAAAA 1327

Qy     721 ccttcaaagagatcatctgttgctat 746
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Db    1328 CCTTCAAAGAGATCATCTGTTGCTAT 1353
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RESULT 7
US-08-780-749A-5
; Sequence 5, Application US/08780749A
; Patent No. 5932779
; GENERAL INFORMATION:
; APPLICANT: Lee, Frank
; APPLICANT: Huszar, Dennis
; APPLICANT: Gu, Wei

```
;    TITLE OF INVENTION:  SCREENING METHODS FOR COMPOUNDS
;    TITLE OF INVENTION:  USEFUL IN THE REGULATION OF BODY WEIGHT
;    NUMBER OF SEQUENCES:  10
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Pennie & Edmonds LLP
;      STREET:  1155 Avenue of the Americas
;      CITY:  New York
;      STATE:  New York
;      COUNTRY:  USA
;      ZIP:  10036/2711
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Diskette
;      COMPUTER:  IBM Compatible
;      OPERATING SYSTEM:  DOS
;      SOFTWARE:  FastSEQ Version 2.0
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/780,749A
;      FILING DATE:  08-JAN-1997
;      CLASSIFICATION:  800
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Laura A. Coruzzi
;      REGISTRATION NUMBER:  30,742
;      REFERENCE/DOCKET NUMBER:  7853-064
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (212) 790-9090
;      TELEFAX:  (212) 869-8864/9741
;      TELEX:  66141 PENNIE
;  INFORMATION FOR SEQ ID NO:  5:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  1671 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    FEATURE:
;      NAME/KEY:  Coding Sequence
;      LOCATION:  394...1389
;      OTHER INFORMATION:
US-08-780-749A-5


  Query Match             87.7%;  Score 654.4;  DB 2;  Length 1671;
  Best Local Similarity   92.2%;  Pred. No. 3.2e-177;
  Matches  688;  Conservative    1;  Mismatches   57;  Indels    0;  Gaps    0;

Qy       1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Db     608 ACAAGAATCTGCATTCACCCATGTACTTTTTCATCTGCAGCTTGGCTGTGGCTGATATGC 667

Qy      61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
           |||||||||||||| ||||| |||||||||||| |||||||||||||||||||| || || |
Db     668 TGGTGAGCGTTTCAAATGGATCAGAAACCATTATCATCACCCTATTAAACAGTACAGATA 727

Qy     121 cggacgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgtagct 180
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Db     728 CGGATGCACAGAGTTTCACAGTGAATATTGATAATGTCATTGACTCGGTGATCTGTAGCT 787

Qy     181 ccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttactatct 240
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Db    788 CCTTGCTTGCATCCATTTGCAGCCTGCTTTCAATTGCAGTGGACAGGTACTTTACTATCT 847

Qy    241 tttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatcagtt 300
          | |||||||||||||||||||||||||||||||||||||||||||||||| |||| ||| ||||
Db    848 TCTATGCTCTCCAGTACCATAACATTATGACAGTTAAGCGGGTTGGGATCAGCATAAGTT 907

Qy    301 gtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagcagtg 360
          |||||||||||  |||||||| || ||  |||||||||||||||||||||||| ||||
Db    908 GTATCTGGGCAGCTTGCACGGTTTCAGGCATTTTGTTCATCATTTACTCAGATAGTAGTG 967

Qy    361 ctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctctct 420
          |||| || |||||||||| ||| ||||||||||||||||||||||||||||||||||||
Db    968 CTGTCATCATCTGCCTCATCACCATGTTCTTCACCATGCTGGCTCTCATGGCTTCTCTCT 1027

Qy    421 atgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccaggca 480
          |||||||||||||||| |||||||| || |||||||||||||| || |||||||| ||||
Db   1028 ATGTCCACATGTTCCTGATGGCCAGGCTTCACATTAAGAGGATTGCTGTCCTCCCCGGCA 1087

Qy    481 ctggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttgattg 540
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Db   1088 CTGGTGCCATCCGCCAAGGTGCCAATATGAAGGGAGCGATTACCTTGACCATCCTGATTG 1147

Qy    541 gggtctttgtggtctgctgggccccttcttcctccacttaatattctatatctcctgcc 600
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Db   1148 GCGTCTTTGTTGTCTGCTGGGCCCCATTCTTCCTCCACTTAATATTCTACATCTCTTGTC 1207

Qy    601 cccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctcatcctgatca 660
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Db   1208 CTCAGAATCCATATTGTGTGTGCTTCATGTCTCACTTTAACTTGTATCTCATACTGATCA 1267

Qy    661 tgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgaggaaaa 720
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Db   1268 TGTGTAATTCAATCATCGATCCTCTGATTTATGCACTCCGGAGTCAAGAACTGAGGAAAA 1327

Qy    721 ccttcaaagagatcatctgttgctat 746
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Db   1328 CCTTCAAAGAGATCATCTGTTGCTAT 1353
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RESULT 8
US-08-706-281A-15
; Sequence 15, Application US/08706281A
; Patent No. 6100048
; GENERAL INFORMATION:
; APPLICANT: Cone, Roger D
; APPLICANT: Fan, Wei
; APPLICANT: Boston, Bruce A
; APPLICANT: Kesterton, Robert A
; APPLICANT: Lu, Dongsi
; APPLICANT: Chen, Wenbiao
; TITLE OF INVENTION: Methods and Reagents for Discovering and
; TITLE OF INVENTION: Using Mammalian Melanocortin Receptor Agonists and
Antagonists
; TITLE OF INVENTION: To Modulate Feeding Behavior in Animals
; NUMBER OF SEQUENCES: 19
; CORRESPONDENCE ADDRESS:

; ADDRESSEE: McDonnell Boehnen Hulbert & Berghoff
; STREET: 300 South Wacker Drive
; CITY: Chicago
; STATE: IL
; COUNTRY: USA
; ZIP: 60606
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/706,281A
; FILING DATE: 04-SEP-1996
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: No. 6100048nan, Kevin E
; REGISTRATION NUMBER: 35,303
; REFERENCE/DOCKET NUMBER: 96,886
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 312-913-0001
; TELEFAX: 312-913-0002
; TELEX:
; INFORMATION FOR SEQ ID NO: 15:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 1671 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: cDNA to mRNA
; FEATURE:
; NAME/KEY: 5'UTR
; LOCATION: 1..393
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 394..1389
; FEATURE:
; NAME/KEY: 3'UTR
; LOCATION: 1390..1671
US-08-706-281A-15

Query Match 87.1%; Score 649.6; DB 3; Length 1671;
Best Local Similarity 91.8%; Pred. No. 7.5e-176;
Matches 685; Conservative 1; Mismatches 60; Indels 0; Gaps 0;

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Qy      1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Db    608 ACAAGAATCTGCATTCACCCATGTACTTTTTCATCTGCAGCTTGGCTGTGGCTGATATGC 667

Qy     61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
          |||||||||||||| ||||| |||||||||||| |||||||||||||||| | || || |
Db    668 TGGTGAGCGTTTCAAATGGATCAGAAACCATTATCATCACCCTATTAAACCGTACAGATA 727

Qy    121 cggacgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgtagct 180
          |||| ||||||||||||||||||||||||||||||||||||| ||||||||||||
Db    728 CGGATGCACAGAGTTTCACAGTGAATATTGATAATGTCATTGACTCGGTGATCTGTAGCT 787
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Qy    181 ccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttactatct 240
          |||| || || || |||||||||||||||| |||||||||||||||| ||||||||||
Db    788 CCTTGCTTGCATCCATTTGCAGCCTGCTTTCAATTGCAGTGGACAGGTACTTTACTATCT 847

Qy    241 tttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatcagtt 300
          | |||||||||||||||||||||||||||||||||||||||||||| |||| ||| ||||
Db    848 TCTATGCTCTCCAGTACCATAACATTATGACAGTTAAGCGGGTTGGGATCAGCATAAGTT 907

Qy    301 gtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagcagtg 360
          |||||||||||  |||||||| || ||| |||||||||||||||||||||||| ||||
Db    908 GTATCTGGGCAGCTTGCACGGTTTCAGGTATTTTGTTCATCATTTACTCAGATAGTAGTG 967

Qy    361 ctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctctct 420
          |||| || |||||||||| ||| ||||||||||||||||||||||||||||||||||||
Db    968 CTGTCATCATCTGCCTCATCACCATGTTCTTCACCATGCTGGCTCTCATGGCTTCTCTCT 1027

Qy    421 atgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccaggca 480
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Db   1028 ATGTCCACCTGTTCCTGATGGCCAGGCTTCACATTAAGAGGATTGCTGTCCTCCCCGGCA 1087

Qy    481 ctggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttgattg 540
          ||||  |||||||||||||||||| |||||||| || |||||| |||||||| ||||||
Db   1088 CTGGTGCCATCCGCCAAGGTGCCAATATGAAGGGAGCGATTACCTTGACCATCCTGATTG 1147

Qy    541 gggtctttgtggtctgctgggccccttcttcctccacttaatattctatatctcctgcc 600
          | |||||||| |||||||||||||| |||||||||||||||||||||| ||||| || |
Db   1148 GCGTCTTTGTTGTCTGCTGGGCCCCATTCTTCCTCCACTTAATATTCTACATCTCTTGTC 1207

Qy    601 cccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctcatcctgatca 660
          | |||||||||||  |||||||||||||||||||||||||| |||||||||||  |||||||
Db   1208 CTCAGAATCCATATTGTGTGTGCTTCATGTCTCACTTTAACTTGTATCTCATACTGATCA 1267

Qy    661 tgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgaggaaaa 720
          ||||||||||  ||||||:|||| |||||||||||||||||||| ||||||||||||||||
Db   1268 TGTGTAATTCAATCATCGATCCTCTGATTTATGCACTCCGGAGTCAAGAACTGAGGAAAA 1327

Qy    721 ccttcaaagagatcatctgttgctat 746
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Db   1328 CCTTCAAAGAGATCATCTCTTCCTAT 1353
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RESULT 9
US-08-671-525B-9
; Sequence 9, Application US/08671525B
; Patent No. 5703220
; GENERAL INFORMATION:
; APPLICANT: Yamada, Tadataka
; APPLICANT: Gantz, Ira
; TITLE OF INVENTION: Genes Encoding Melanocortin Receptors
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Harness, Dickey & Pierce, P.L.C.
; STREET: P.O. Box 828
; CITY: Bloomfield Hills
; STATE: MI
; COUNTRY: US

; ZIP: 48303
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/671,525B
; FILING DATE: June 27, 1996
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Smith, DeAnn F.
; REGISTRATION NUMBER: 36683
; REFERENCE/DOCKET NUMBER: 2115-000853DVB
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (810)641-1600
; TELEFAX: (810)641-0270
; INFORMATION FOR SEQ ID NO: 9:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 975 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: double
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; ORIGINAL SOURCE:
; ORGANISM: Mouse
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 1..975
US-08-671-525B-9

Query Match 46.6%; Score 347.8; DB 1; Length 975;
Best Local Similarity 67.5%; Pred. No. 5.3e-90;
Matches 503; Conservative 1; Mismatches 238; Indels 3; Gaps 1;

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Qy      1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Db    191 ACAAAAACCTGCACTCACCCATGTACTTCTATGTGGGCAGCTTAGCCGTGGCCGACATGC 250

Qy     61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
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Db    251 TGGTGAGCATGTCCAATGCCTGGGAGACTGTCACCATATACTTGCTAAATAATAAACACC 310

Qy    121 cgg---acgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgta 177
           ||     ||  | |  ||        | || || || ||  | |||||  ||||||| |
Db    311 TGGTGATAGCCGACACCTTTGTGCGACACATCGACAACGTGTTCGACTCCATGATCTGCA 370

Qy    178 gctccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttacta 237
           |||  |  | ||||| || |||||  ||||  | ||||| ||||||||||  | || |
Db    371 TCTCTGTGGTGGCCTCGATGTGCAGTTTGCTGGCCATTGCGGTGGACAGGTACATCACCA 430

Qy    238 tcttttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatca 297
          |||| |||||  | |  |||||  |||| ||||| |  | |||    ||  | ||||||
Db    431 TCTTCTATGCCTTGCGCTACCACCACATCATGACCGCGAGGCGCTCGGGGGTGATCATCG 490
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Qy    298 gttgtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagca 357
          || |||||| |  ||||||     |  ||  || | |||||||| ||||  ||   ||
Db    491 CCTGCATCTGGACCTTCTGCATAAGCTGCGGCATTGTTTTCATCATCTACTATGAGTCCA 550

Qy    358 gtgctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctc 417
            ||| || || ||||||||  || ||||||||||||||||    ||||||  ||||
Db    551 AGTATGTGATCATTTGCCTCATCTCCATGTTCTTCACCATGCTGTTCTTCATGGTGTCTC 610

Qy    418 tctatgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccag 477
          | ||| | ||||||||||||| ||||| |   |||  | ||| |||| || |    |||
Db    611 TGTATATACACATGTTCCTCCTGGCCCGGAACCATGTCAAGCGGATAGCAGCTTCCCCCA 670

Qy    478 gcactggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttga 537
          |      | || |  | ||| |  ||| |||||||||||| |||||||| |||||  |
Db    671 GATACAACTCCGTGAGGCAAAGGACCAGCATGAAGGGGGCTATTACCCTCACCATGCTAC 730

Qy    538 ttggggtctttgtggtctgctgggccccttcttcctccacttaatattctatatctcct 597
          | ||| | ||  | ||||||||| | |||||||| || ||| | || ||    |||||||
Db    731 TGGGGATTTTCATTGTCTGCTGGTCTCCCTTCTTTCTTCACCTTATCTTAATGATCTCCT 790

Qy    598 gcccccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctcatcctga 657
          |||| |||||    |||||    ||||| |||||| |||| ||  |||| || || || |
Db    791 GCCCTCAGAACGTCTACTGCTCTTGCTTTATGTCTTACTTCAACATGTACCTTATACTCA 850

Qy    658 tcatgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgagga 717
          ||||||| || ||| | |||:|||| || || || || ||||| ||||||||  || |||
Db    851 TCATGTGCAACTCCGTGATCGATCCTCTCATCTACGCCCTCCGCAGCCAAGAGATGCGGA 910

Qy    718 aaaccttcaaagagatcatctgttg 742
            ||||| || |||||| |||||||
Db    911 GGACCTTTAAGGAGATCGTCTGTTG 935
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RESULT 10
US-08-672-109B-9
; Sequence 9, Application US/08672109B
; Patent No. 5710265
; GENERAL INFORMATION:
; APPLICANT: Yamada, Tadataka
; APPLICANT: Gantz, Ira
; TITLE OF INVENTION: Genes Encoding Melanocortin Receptors
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Harness, Dickey & Pierce, P.L.C.
; STREET: P.O. Box 828
; CITY: Bloomfield Hills
; STATE: MI
; COUNTRY: US
; ZIP: 48303
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/672,109B

; FILING DATE: June 27, 1996
; CLASSIFICATION: 536
; ATTORNEY/AGENT INFORMATION:
; NAME: Smith, DeAnn F.
; REGISTRATION NUMBER: 36683
; REFERENCE/DOCKET NUMBER: 2115-000853DVC
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (810)641-1600
; TELEFAX: (810)641-0270
; INFORMATION FOR SEQ ID NO: 9:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 975 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: double
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; ORIGINAL SOURCE:
; ORGANISM: Mouse
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 1..975
US-08-672-109B-9

Query Match 46.6%; Score 347.8; DB 1; Length 975;
Best Local Similarity 67.5%; Pred. No. 5.3e-90;
Matches 503; Conservative 1; Mismatches 238; Indels 3; Gaps 1;

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Qy      1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Db    191 ACAAAAACCTGCACTCACCCATGTACTTCTATGTGGGCAGCTTAGCCGTGGCCGACATGC 250

Qy     61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
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Db    251 TGGTGAGCATGTCCAATGCCTGGGAGACTGTCACCATATACTTGCTAAATAATAAACACC 310

Qy    121 cgg---acgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgta 177
           ||     ||  | |  ||        | || || || ||  | |||||  ||||||| |
Db    311 TGGTGATAGCCGACACCTTTGTGCGACACATCGACAACGTGTTCGACTCCATGATCTGCA 370

Qy    178 gctccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttacta 237
           |||  |  | ||||| || |||||  ||||  | ||||| ||||||||||  | || |
Db    371 TCTCTGTGGTGGCCTCGATGTGCAGTTTGCTGGCCATTGCGGTGGACAGGTACATCACCA 430

Qy    238 tcttttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatca 297
          |||| |||||  | |  |||||  |||| ||||| |  | |||    ||  | ||||||
Db    431 TCTTCTATGCCTTGCGCTACCACCACATCATGACCGCGAGGCGCTCGGGGGTGATCATCG 490

Qy    298 gttgtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagca 357
            || |||||| |  ||||||      |  ||  || | |||||||| ||||  ||   ||
Db    491 CCTGCATCTGGACCTTCTGCATAAGCTGCGGCATTGTTTTCATCATCTACTATGAGTCCA 550

Qy    358 gtgctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctc 417
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Db    551 AGTATGTGATCATTTGCCTCATCTCCATGTTCTTCACCATGCTGTTCTTCATGGTGTCTC 610
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Qy    418 tctatgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccag 477
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Db    611 TGTATATACACATGTTCCTCCTGGCCCGGAACCATGTCAAGCGGATAGCAGCTTCCCCCA 670

Qy    478 gcactggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttga 537
          |      | || |  | ||| |  ||| |||||||||||| |||||||| |||||  |
Db    671 GATACAACTCCGTGAGGCAAAGGACCAGCATGAAGGGGGCTATTACCCTCACCATGCTAC 730

Qy    538 ttggggtctttgtggtctgctgggccccttcttcctccacttaatattctatatctcct 597
          | ||| | ||  | |||||||||| | |||||||| || ||| | || ||    |||||||
Db    731 TGGGGATTTTCATTGTCTGCTGGTCTCCCTTCTTTCTTCACCTTATCTTAATGATCTCCT 790

Qy    598 gcccccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctcatcctga 657
          |||| |||||    |||||    ||||| |||||| |||| ||  |||| || || || |
Db    791 GCCCTCAGAACGTCTACTGCTCTTGCTTTATGTCTTACTTCAACATGTACCTTATACTCA 850

Qy    658 tcatgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgagga 717
          ||||||| || ||| | |||:|||| || || || || ||||| |||||||| || |||
Db    851 TCATGTGCAACTCCGTGATCGATCCTCTCATCTACGCCCTCCGCAGCCAAGAGATGCGGA 910

Qy    718 aaaccttcaaagagatcatctgttg 742
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Db    911 GGACCTTTAAGGAGATCGTCTGTTG 935
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RESULT 11
US-08-842-045-9
; Sequence 9, Application US/08842045
; Patent No. 5817787
; GENERAL INFORMATION:
; APPLICANT: Yamada, Tadataka
; APPLICANT: Gantz, Ira
; TITLE OF INVENTION: Genes Encoding Melanocortin Receptors
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Harness, Dickey & Pierce, P.L.C.
; STREET: P.O. Box 828
; CITY: Bloomfield Hills
; STATE: MI
; COUNTRY: US
; ZIP: 48303
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/842,045
; FILING DATE:
; CLASSIFICATION: 536
; ATTORNEY/AGENT INFORMATION:
; NAME: Smith, DeAnn F.
; REGISTRATION NUMBER: 36683
; REFERENCE/DOCKET NUMBER: 2115-000853DVE
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (810)641-1600

; TELEFAX: (810)641-0270
; INFORMATION FOR SEQ ID NO: 9:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 975 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: double
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; ORIGINAL SOURCE:
; ORGANISM: Mouse
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 1..975
US-08-842-045-9

Query Match 46.6%; Score 347.8; DB 1; Length 975;
Best Local Similarity 67.5%; Pred. No. 5.3e-90;
Matches 503; Conservative 1; Mismatches 238; Indels 3; Gaps 1;

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Qy      1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Db    191 ACAAAAACCTGCACTCACCCATGTACTTCTATGTGGGCAGCTTAGCCGTGGCCGACATGC 250

Qy     61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
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Db    251 TGGTGAGCATGTCCAATGCCTGGGAGACTGTCACCATATACTTGCTAAATAATAAACACC 310

Qy    121 cgg---acgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgta 177
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Db    311 TGGTGATAGCCGACACCTTTGTGCGACACATCGACAACGTGTTCGACTCCATGATCTGCA 370

Qy    178 gctccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtatttttacta 237
           |||   |   |  |||||  ||  |||||   ||||   |  |||||  ||||||||||||   |  ||  |
Db    371 TCTCTGTGGTGGCCTCGATGTGCAGTTTGCTGGCCATTGCGGTGGACAGGTACATCACCA 430

Qy    238 tcttttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatca 297
          ||||  |||||   |  |   |||||   ||||  |||||  |   |  |||     ||   |  ||||||
Db    431 TCTTCTATGCCTTGCGCTACCACCACATCATGACCGCGAGGCGCTCGGGGGTGATCATCG 490

Qy    298 gttgtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagca 357
            ||  ||||||  |   ||||||      |   ||   ||  |  ||||||||  ||||   ||    ||
Db    491 CCTGCATCTGGACCTTCTGCATAAGCTGCGGCATTGTTTTCATCATCTACTATGAGTCCA 550

Qy    358 gtgctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctc 417
              |||  ||  ||  ||||||||   ||  ||||||||||||||||     ||||||   ||||
Db    551 AGTATGTGATCATTTGCCTCATCTCCATGTTCTTCACCATGCTGTTCTTCATGGTGTCTC 610

Qy    418 tctatgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccag 477
          |  |||  |  ||||||||||||  |||||  |    |||   |  |||  ||||  ||  |     |||
Db    611 TGTATATACACATGTTCCTCCTGGCCCGGAACCATGTCAAGCGGATAGCAGCTTCCCCCA 670

Qy    478 gcadtggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttga 537
          |       | ||  |   | |||  |   |||  ||||||||||||  ||||||||  |||||   |
Db    671 GATACAACTCCGTGAGGCAAAGGACCAGCATGAAGGGGGCTATTACCCTCACCATGCTAC 730
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Qy     538 ttggggtctttgtggtctgctgggccccttcttcctccacttaatattctatatctcct 597
           | ||| | ||  | ||||||||| | |||||||| || ||| | || ||    |||||||
Db     731 TGGGGATTTTCATTGTCTGCTGGTCTCCCTTCTTTCTTCACCTTATCTTAATGATCTCCT 790

Qy     598 gcccccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctcatcctga 657
           |||| |||||    |||||    ||||| |||||| |||| ||  |||| || || || |
Db     791 GCCCTCAGAACGTCTACTGCTCTTGCTTTATGTCTTACTTCAACATGTACCTTATACTCA 850

Qy     658 tcatgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgagga 717
           ||||||| || ||| | |||:|||| || || || || ||||| |||||||  || |||
Db     851 TCATGTGCAACTCCGTGATCGATCCTCTCATCTACGCCCTCCGCAGCCAAGAGATGCGGA 910

Qy     718 aaaccttcaaagagatcatctgttg 742
             ||||| || |||||| |||||||
Db     911 GGACCTTTAAGGAGATCGTCTGTTG 935
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RESULT 12
US-08-842-238-9
; Sequence 9, Application US/08842238
; Patent No. 5869257
; GENERAL INFORMATION:
; APPLICANT: Yamada, Tadataka
; APPLICANT: Gantz, Ira
; TITLE OF INVENTION: Genes Encoding Melanocortin Receptors
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Harness, Dickey & Pierce, P.L.C.
; STREET: P.O. Box 828
; CITY: Bloomfield Hills
; STATE: MI
; COUNTRY: US
; ZIP: 48303
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/842,238
; FILING DATE:
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Smith, DeAnn F.
; REGISTRATION NUMBER: 36683
; REFERENCE/DOCKET NUMBER: 2115-000853DVD
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (810)641-1600
; TELEFAX: (810)641-0270
; INFORMATION FOR SEQ ID NO: 9:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 975 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: double
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)

; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; ORIGINAL SOURCE:
; ORGANISM: Mouse
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 1..975
US-08-842-238-9

Query Match 46.6%; Score 347.8; DB 2; Length 975;
Best Local Similarity 67.5%; Pred. No. 5.3e-90;
Matches 503; Conservative 1; Mismatches 238; Indels 3; Gaps 1;

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Qy      1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Db    191 ACAAAAACCTGCACTCACCCATGTACTTCTATGTGGGCAGCTTAGCCGTGGCCGACATGC 250

Qy     61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
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Db    251 TGGTGAGCATGTCCAATGCCTGGGAGACTGTCACCATATACTTGCTAAATAATAAACACC 310

Qy    121 cgg---acgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgta 177
           ||     ||  | |  ||        | ||  ||  ||  ||  |  |||||  |||||||  |
Db    311 TGGTGATAGCCGACACCTTTGTGCGACACATCGACAACGTGTTCGACTCCATGATCTGCA 370

Qy    178 gctccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttacta 237
           |||  |  | |||||  ||  |||||  ||||  | |||||  ||||||||||||  | ||  |
Db    371 TCTCTGTGGTGGCCTCGATGTGCAGTTTGCTGGCCATTGCGGTGGACAGGTACATCACCA 430

Qy    238 tcttttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatca 297
          ||||  |||||  | |  |||||  ||||  |||||  |  | |||    ||  | ||||||
Db    431 TCTTCTATGCCTTGCGCTACCACCACATCATGACCGCGAGGCGCTCGGGGGTGATCATCG 490

Qy    298 gttgtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagca 357
            || ||||||  |  ||||||     |  ||  || | ||||||||  ||||  ||   ||
Db    491 CCTGCATCTGGACCTTCTGCATAAGCTGCGGCATTGTTTTCATCATCTACTATGAGTCCA 550

Qy    358 gtgctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctc 417
             |||  ||  ||  ||||||||  ||  ||||||||||||||||    ||||||  ||||
Db    551 AGTATGTGATCATTTGCCTCATCTCCATGTTCTTCACCATGCTGTTCTTCATGGTGTCTC 610

Qy    418 tctatgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccag 477
          | |||  | ||||||||||||  |||||  |   |||   |  |||  ||||  ||  |    |||
Db    611 TGTATATACACATGTTCCTCCTGGCCCGGAACCATGTCAAGCGGATAGCAGCTTCCCCCA 670

Qy    478 gcactggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttga 537
          |      | ||  |  | |||  |  |||  ||||||||||||  ||||||||  |||||  |
Db    671 GATACAACTCCGTGAGGCAAAGGACCAGCATGAAGGGGGCTATTACCCTCACCATGCTAC 730

Qy    538 ttggggtctttgtggtctgctgggcccccttcttcctccacttaatattctatatctcct 597
          | |||  |  ||   |  |||||||||  |  ||||||||  ||  |||  |  ||  ||    |||||||
Db    731 TGGGGATTTTCATTGTCTGCTGGTCTCCCTTCTTTCTTCACCTTATCTTAATGATCTCCT 790

Qy    598 gcccccagaatccatactgtgtgtgcttcatgtctcacttaatttgtatctcatcctga 657
          ||||  |||||    |||||    |||||  ||||||  ||||  ||  ||||  ||  ||  ||  |
Db    791 GCCCTCAGAACGTCTACTGCTCTTGCTTTATGTCTTACTTCAACATGTACCTTATACTCA 850
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Qy     658 tcatgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgagga 717
           ||||||| || ||| | |||:|||| || || || || ||||| ||||||||  || |||
Db     851 TCATGTGCAACTCCGTGATCGATCCTCTCATCTACGCCCTCCGCAGCCAAGAGATGCGGA 910

Qy     718 aaaccttcaaagagatcatctgttg 742
             ||||| || |||||| |||||||
Db     911 GGACCTTTAAGGAGATCGTCTGTTG 935
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RESULT 13
US-08-629-335B-9
; Sequence 9, Application US/08629335B
; Patent No. 6117975
; GENERAL INFORMATION:
; APPLICANT: Yamada, Tadataka
; APPLICANT: Gantz, Ira
; TITLE OF INVENTION: Genes Encoding Melanocortin Receptors
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Harness, Dickey & Pierce, P.L.C.
; STREET: P.O. Box 828
; CITY: Bloomfield Hills
; STATE: MI
; COUNTRY: US
; ZIP: 48303
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/629,335B
; FILING DATE: July 23, 1996
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Smith, DeAnn F.
; REGISTRATION NUMBER: 36683
; REFERENCE/DOCKET NUMBER: 2115-000853DVA
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (810)641-1600
; TELEFAX: (810)641-0270
; INFORMATION FOR SEQ ID NO: 9:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 975 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: double
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; ORIGINAL SOURCE:
; ORGANISM: Mouse
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 1..975
US-08-629-335B-9

Query Match 46.6%; Score 347.8; DB 3; Length 975;
Best Local Similarity 67.5%; Pred. No. 5.3e-90;
Matches 503; Conservative 1; Mismatches 238; Indels 3; Gaps 1;

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Qy      1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Qy     61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
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Db    251 TGGTGAGCATGTCCAATGCCTGGGAGACTGTCACCATATACTTGCTAAATAATAAACACC 310

Qy    121 cgg---acgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgta 177
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Db    311 TGGTGATAGCCGACACCTTTGTGCGACACATCGACAACGTGTTCGACTCCATGATCTGCA 370

Qy    178 gctccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttacta 237
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Db    371 TCTCTGTGGTGGCCTCGATGTGCAGTTTGCTGGCCATTGCGGTGGACAGGTACATCACCA 430

Qy    238 tcttttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatca 297
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Db    431 TCTTCTATGCCTTGCGCTACCACCACATCATGACCGCGAGGCGCTCGGGGGTGATCATCG 490

Qy    298 gttgtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagca 357
            || ||||||  |  ||||||     |  ||  ||  | ||||||||  ||||  ||   ||
Db    491 CCTGCATCTGGACCTTCTGCATAAGCTGCGGCATTGTTTTCATCATCTACTATGAGTCCA 550

Qy    358 gtgctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctc 417
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Db    551 AGTATGTGATCATTTGCCTCATCTCCATGTTCTTCACCATGCTGTTCTTCATGGTGTCTC 610

Qy    418 tctatgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccag 477
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Db    611 TGTATATACACATGTTCCTCCTGGCCCGGAACCATGTCAAGCGGATAGCAGCTTCCCCCA 670

Qy    478 gcactggcaccatccgccaaggtgccaacatgaaggggcaattaccctgaccatcttga 537
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Db    671 GATACAACTCCGTGAGGCAAAGGACCAGCATGAAGGGGGCTATTACCCTCACCATGCTAC 730

Qy    538 ttggggtctttgtggtctgctgggcccccttcttcctccacttaatattctatatctcct 597
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Db    731 TGGGGATTTTCATTGTCTGCTGGTCTCCCTTCTTTCTTCACCTTATCTTAATGATCTCCT 790

Qy    598 gcccccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctcatcctga 657
          ||||  |||||    |||||    |||||  ||||||  ||||  ||  ||||  ||  ||  ||  |
Db    791 GCCCTCAGAACGTCTACTGCTCTTGCTTTATGTCTTACTTCAACATGTACCTTATACTCA 850

Qy    658 tcatgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgagga 717
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Db    851 TCATGTGCAACTCCGTGATCGATCCTCTCATCTACGCCCTCCGCAGCCAAGAGATGCGGA 910

Qy    718 aaaccttcaaagagatcatctgttg 742
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Db    911 GGACCTTTAAGGAGATCGTCTGTTG 935
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RESULT 14
US-08-706-281A-17
; Sequence 17, Application US/08706281A
; Patent No. 6100048
; GENERAL INFORMATION:
; APPLICANT: Cone, Roger D
; APPLICANT: Fan, Wei
; APPLICANT: Boston, Bruce A
; APPLICANT: Kesterton, Robert A
; APPLICANT: Lu, Dongsi
; APPLICANT: Chen, Wenbiao
; TITLE OF INVENTION: Methods and Reagents for Discovering and
; TITLE OF INVENTION: Using Mammalian Melanocortin Receptor Agonists and
Antagonists
; TITLE OF INVENTION: To Modulate Feeding Behavior in Animals
; NUMBER OF SEQUENCES: 19
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: McDonnell Boehnen Hulbert & Berghoff
; STREET: 300 South Wacker Drive
; CITY: Chicago
; STATE: IL
; COUNTRY: USA
; ZIP: 60606
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/706,281A
; FILING DATE: 04-SEP-1996
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: No. 6100048nan, Kevin E
; REGISTRATION NUMBER: 35,303
; REFERENCE/DOCKET NUMBER: 96,886
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 312-913-0001
; TELEFAX: 312-913-0002
; TELEX:
; INFORMATION FOR SEQ ID NO: 17:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 978 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 1..975
US-08-706-281A-17

Query Match 46.4%; Score 346.2; DB 3; Length 978;
Best Local Similarity 67.4%; Pred. No. 1.5e-89;

Matches 502; Conservative 1; Mismatches 239; Indels 3; Gaps 1;

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Db    191 ACAAAAACCTGCACTCACCCATGTACTTCTTTGTGGGCAGCTTAGCCGTGGCCGACATGC 250

Qy     61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggaca 120
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Db    251 TGGTGAGCATGTCCAATGCCTGGGAGACTGTCACCATATACTTGCTAAATAATAAACACC 310

Qy    121 cgg---acgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgta 177
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Db    311 TGGTGATAGCCGACACCTTTGTGCGACACATCGACAACGTGTTCGACTCCATGATCTGCA 370

Qy    178 gctccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttacta 237
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Db    371 TCTCTGTGGTGGCCTCGATGTGCAGTTTGCTGGCCATTGCGGTGGATAGGTACATCACCA 430

Qy    238 tcttttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatca 297
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Db    431 TCTTCTATGCCTTGCGCTACCACCACATCATGACCGCGAGGCGCTCGGGGGTGATCATCG 490

Qy    298 gttgtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagca 357
            || || ||| |  ||||||     |  ||  || | |||||||| ||||  ||   ||
Db    491 CCTGCATTTGGACCTTCTGCATAAGCTGCGGCATTGTTTTCATCATCTACTATGAGTCCA 550

Qy    358 gtgctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctc 417
              ||| || || ||||||||  || ||||||||||||||||,  ||||||  ||||
Db    551 AGTATGTGATCATTTGCCTCATCTCCATGTTCTTCACCATGCTGTTCTTCATGGTGTCTC 610

Qy    418 tctatgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctcccag 477
          | ||| | |||||||||||| |||||  |   |||  | ||| |||| || |    |||
Db    611 TGTATATACACATGTTCCTCCTGGCCCGGAACCATGTCAAGCGGATAGCAGCTTCCCCCA 670

Qy    478 gcactggcaccatccgccaaggtgccaacatgaagggggcaattaccctgaccatcttga 537
          |      | || |  | ||| |  ||| |||||||||||| |||||||| |||||  |
Db    671 GATACAACTCCGTGAGGCAAAGGACCAGCATGAAGGGGGCTATTACCCTCACCATGCTAC 730

Qy    538 ttggggtctttgtggtctgctgggccccctttcttcctccacttaatattctatatctcct 597
          | ||| | ||  | |||||||| | |||||||| || ||| | || ||    |||||||
Db    731 TGGGGATTTTCATTGTCTGCTGGTCTCCCTTCTTTCTTCACCTTATCTTAATGATCTCCT 790

Qy    598 gcccccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctcatcctga 657
          |||| |||||    |||||    ||||| |||||| |||| ||  |||| || || || |
Db    791 GCCCTCAGAACGTCTACTGCTCTTGCTTTATGTCTTACTTCAACATGTACCTTATACTCA 850

Qy    658 tcatgtgtaattccatcatcratcccctgatttatgcactccggagccaagaactgagga 717
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Db    851 TCATGTGCAACTCCGTGATCGATCCTCTCATCTACGCCCTCCGCAGCCAAGAGATGCGGA 910

Qy    718 aaaccttcaaagagatcatctgttg 742
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Db    911 GGACCTTTAAGGAGATCGTCTGTTG 935
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RESULT 15
US-08-671-525B-5

; Sequence 5, Application US/08671525B
; Patent No. 5703220
; GENERAL INFORMATION:
; APPLICANT: Yamada, Tadataka
; APPLICANT: Gantz, Ira
; TITLE OF INVENTION: Genes Encoding Melanocortin Receptors
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Harness, Dickey & Pierce, P.L.C.
; STREET: P.O. Box 828
; CITY: Bloomfield Hills
; STATE: MI
; COUNTRY: US
; ZIP: 48303
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/671,525B
; FILING DATE: June 27, 1996
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Smith, DeAnn F.
; REGISTRATION NUMBER: 36683
; REFERENCE/DOCKET NUMBER: 2115-000853DVB
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (810)641-1600
; TELEFAX: (810)641-0270
; INFORMATION FOR SEQ ID NO: 5:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 1080 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: double
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; ORIGINAL SOURCE:
; ORGANISM: Homo sapiens
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 1..1080
US-08-671-525B-5

Query Match 42.8%; Score 319.4; DB 1; Length 1080;
Best Local Similarity 65.9%; Pred. No. 6.8e-82;
Matches 496; Conservative 1; Mismatches 247; Indels 9; Gaps 2;

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Qy       1 acaagaatctgcattcacccatgtacttttttcatctgtagcctggctgtggctgatatgc 60
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Db     308 ACGGCAACCTGCACTCCCCGATGTACTTCTTTCTCTGCAGCCTGGCGGTGGCCGACATGC 367

Qy      61 tggtgagcgtttccaatgggtcagaaaccattgtcatcaccctattaaacagcacggac- 119
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Db    368 TGGTAAGTGTGTCCAATGCCCTGGAGACCATCATGATCGCCATCGTCCACAGCGACTACC 427

Qy    120 --acggacgcacagagtttcacagtgaatattgataatgtcattgactcagtgatctgta 177
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Db    428 TGACCTTCGAGGACCAGTTTATCCAGCACATGGACAACATCTTCGACTCCATGATCTGCA 487

Qy    178 gctccttactcgcctcaatttgcagcctgctttcgattgcagtggacaggtattttacta 237
           |||| |  | ||||| || |||| ||| ||  | || || || ||||||||  | || |
Db    488 TCTCCCTGGTGGCCTCCATCTGCAACCTCCTGGCCATCGCCGTCGACAGGTACGTCACCA 547

Qy    238 tcttttatgctctccagtaccataacattatgacagttaagcgggttggaatcatcatca 297
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Db    548 TCTTTTACGCGCTCCGCTACCACAGCATCATGACCGTGAGGAAGGCCCTCACCTTGATCG 607

Qy    298 gttgtatctgggcagtctgcacggtgtcgggtgttttgttcatcatttactcagatagca 357
               |||||||    ||||   || |  || ||  |||||||| | ||||| || ||||
Db    608 TGGCCATCTGGGTCTGCTGCGGCGTCTGTGGCGTGGTGTTCATCGTCTACTCGGAGAGCA 667

Qy    358 gtgctgttattatctgcctcataaccgtgttcttcaccatgctggctctcatggcttctc 417
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Db    668 AAATGGTCATTGTGTGCCTCATCACCATGTTCTTCGCCATGATGCTCCTCATGGGCACCC 727

Qy    418 tctatgtccacatgttcctcatggccagactccacattaagaggatcgccgtcctccca- 476
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Db    728 TCTACGTGCACATGTTCCTCTTTGCGCGGCTGCACGTCAAGCGCATAGCAGCACTGCCAC 787

Qy    477 -----ggcactggcaccatccgccaaggtgccaacatgaaggggggcaattaccctgacca 531
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Db    788 CTGCCGACGGGGTGGCCCCACAGCAACACTCATGCATGAAGGGGGCAGTCACCATCACCA 847

Qy    532 tcttgattggggtctttgtggtctgctgggcccccttcttcctccacttaatattctata 591
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Db    848 TTCTCCTGGGCGTGTTCATCTTCTGCTGGGCCCCCTTCTTCCTCCACCTGGTCCTCATCA 907

Qy    592 tctcctgcccccagaatccatactgtgtgtgcttcatgtctcactttaatttgtatctca 651
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Db    908 TCACCTGCCCCACCAACCCCTACTGCATCTGCTACACTGCCCACTTCAACACCTACCTGG 967

Qy    652 tcctgatcatgtgtaattccatcatcratcccctgatttatgcactccggagccaagaac 711
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Db    968 TCCTCATCATGTGCAACTCCGTCATCGACCCACTCATCTACGCTTTCCGGAGCCTGGAAT 1027

Qy    712 tgaggaaaaccttcaaagagatcatctgttgct 744
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Search completed: April 5, 2001, 07:06:42
Job time: 5964 sec

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=> fil reg; d stat que

FILE 'REGISTRY' ENTERED AT 15:32:06 ON 09 APR 2001
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DICTIONARY FILE UPDATES:   8 APR 2001  HIGHEST RN 330546-75-3

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  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.


L1             8 SEA FILE=REGISTRY MSHFNLYLILIMCNSIIDPLIYAL/SQSP
L2        941245 SEA FILE=REGISTRY SQL< 50
L3             0 SEA FILE=REGISTRY L1 AND L2


=> fil hcaplu

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FILE COVERS 1967 - 9 Apr 2001  VOL 134 ISS 16
FILE LAST UPDATED: 8 Apr 2001  (20010408/ED)

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 substance identification.

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 all substance data from the REGISTRY file.  Enter HELP FIRST for
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and title searches back to 1907.  The records from 1907-1966 now have
this searchable data in CAOLD.  You now have electronic access to all
of CA: 1907 to 1966 in CAOLD and 1967 to the present in HCAPLUS on STN.


=> d stat que

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L5           4 SEA FILE=REGISTRY L4 AND L2
L10          1 SEA FILE=HCAPLUS L5


=> d ibib abs hitrn l10


L10  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2000:98833  HCAPLUS
DOCUMENT NUMBER:          132:162049
TITLE:                    Porcine melanocortin-4 receptor gene and use as a
                          genetic marker for fat content, weight gain, and/or
                          feed consumption of animals
INVENTOR(S):              Rothschild, Max F.; Larson, Niels J.; Kim, Kwan Suk
PATENT ASSIGNEE(S):       Iowa State University Research Foundation, Inc., USA
SOURCE:                   PCT Int. Appl., 49 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ----------------  ----  --------      ---------------  --------
     WO 2000006777      A2   20000210      WO 1999-US16862  19990726
     WO 2000006777      A3   20000511
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
             JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
             MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9952301         A1   20000221      AU 1999-52301    19990726
PRIORITY APPLN. INFO.:                    US 1998-94287    19980727
                                          US 1999-116186   19990115
                                          WO 1999-US16862  19990726
```

AB Genetic markers in the porcine melanocortin-4 receptor (MC4R) gene are disclosed which are assocd. with fat content, growth rate, and feed consumption. Further, novel sequence data from regions of the gene are disclosed which may be used in a PCR test to screen for the presence of the marker. The genetic marker may be used to screen animals for breeding purposes which have the desired traits regarding fat content, growth rate, and feed consumption. The screening methods disclosed in the invention involve analyzing animals for a polymorphism in the MC4R gene, and test kits which take advantage of the PCR test are also disclosed.

IT **258323-01-2 258323-02-3 258323-03-4**
258323-05-6
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(primer sequence; porcine melanocortin-4 receptor gene and use as a genetic marker for screening animals for polymorphisms assocd. with the desired traits of fat content, wt. gain, and/or feed consumption)

```
=> fil reg

FILE 'REGISTRY' ENTERED AT 15:41:53 ON 09 APR 2001
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STRUCTURE FILE UPDATES:    8 APR 2001  HIGHEST RN 330546-75-3
DICTIONARY FILE UPDATES:   8 APR 2001  HIGHEST RN 330546-75-3

TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> d l5 rn cn lc nte sql kwic can tot


L5   ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2001 ACS
RN   258323-05-6  REGISTRY
CN   DNA, d(A-T-A-G-C-A-A-C-A-G-A-T-G-A-T-C-T-C-T-T-T-G) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   12: PN: WO0006777 SEQID: 11 claimed DNA
LC   STN Files:   CA, CAPLUS, TOXLIT
NTE  singlestranded
SQL  22
SQL  22

SEQ      1 atagcaacag atgatctctt tg
           ========== ========== ==
HITS AT:   1-22

REFERENCE   1:  132:162049

L5   ANSWER 2 OF 4  REGISTRY  COPYRIGHT 2001 ACS
RN   258323-03-4  REGISTRY
CN   DNA, d(C-A-T-T-A-T-G-A-C-A-G-T-T-A-A-G-C-G-G) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   9: PN: WO0006777 SEQID: 9 claimed DNA
LC   STN Files:   CA, CAPLUS, TOXLIT
NTE  singlestranded
SQL  19
SQL  19

SEQ      1 cattatgaca gttaagcgg
           ========== =========
HITS AT:   1-19

REFERENCE   1:  132:162049

L5   ANSWER 3 OF 4  REGISTRY  COPYRIGHT 2001 ACS
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RN 258323-02-3 REGISTRY
CN DNA, d(T-T-A-A-G-T-G-G-A-G-G-A-A-G-A-A-G-G) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 8: PN: WO0006777 SEQID: 8 claimed DNA
LC STN Files: CA, CAPLUS, TOXLIT
NTE singlestranded
SQL **18**
SQL **18**

SEQ 1 ttaagtggag gaagaagg
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HITS AT: 1-18

REFERENCE 1: 132:162049

L5 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2001 ACS
RN 258323-01-2 REGISTRY
CN DNA, d(C-A-G-G-G-G-A-T-A-G-C-A-A-C-A-G-A-T-G-A) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 7: PN: WO0006777 SEQID: 7 claimed DNA
LC STN Files: CA, CAPLUS, TOXLIT
NTE singlestranded
SQL **20**
SQL **20**

SEQ 1 caggggatag caacagatga
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HITS AT: 1-20

REFERENCE 1: 132:162049

=> fil hcaplu

FILE 'HCAPLUS' ENTERED AT 15:52:45 ON 09 APR 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1967 - 9 Apr 2001 VOL 134 ISS 16
FILE LAST UPDATED: 8 Apr 2001 (20010408/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Now you can extend your author, patent assignee, patent information,

and title searches back to 1907. The records from 1907-1966 now have this searchable data in CAOLD. You now have electronic access to all of CA: 1907 to 1966 in CAOLD and 1967 to the present in HCAPLUS on STN.

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=> d stat que l14

L6            3 SEA FILE=REGISTRY ("MELANOCORTIN-4 RECEPTOR (112-METHIONINE)
                (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (137-THREONINE)
                (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (HUMAN)"/CN)
L8          169 SEA FILE=REGISTRY SNP?
L11         254 SEA FILE=HCAPLUS L6 OR MC4R OR MELANOCORTIN(W)4 OR MC4(W)(R OR
                RECEPTOR?)
L12      248593 SEA FILE=HCAPLUS L8 OR SNP?
L14           0 SEA FILE=HCAPLUS L11 AND L12


=> d stat que l15

L6            3 SEA FILE=REGISTRY ("MELANOCORTIN-4 RECEPTOR (112-METHIONINE)
                (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (137-THREONINE)
                (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (HUMAN)"/CN)
L9            1 SEA FILE=REGISTRY TAQI/CN OR "TAQI ENDONUCLEASE"/CN
L11         254 SEA FILE=HCAPLUS L6 OR MC4R OR MELANOCORTIN(W)4 OR MC4(W)(R OR
                RECEPTOR?)
L13        1790 SEA FILE=HCAPLUS L9 OR TAQI OR TAQ(W)I
L15           1 SEA FILE=HCAPLUS L11 AND L13


=> d stat que l16

L2       941245 SEA FILE=REGISTRY SQL< 50
L4           20 SEA FILE=REGISTRY CAGGGGATAGCAACAGATGA|TTAAGTGGAGGAAGAAGG|CATTA
                TGACAGTTAAGCGG|CATTATGACAGTTAAGCGG|ATAGCAACAGATGATCTCTTTG/SQSN
L5            4 SEA FILE=REGISTRY L4 AND L2
L6            3 SEA FILE=REGISTRY ("MELANOCORTIN-4 RECEPTOR (112-METHIONINE)
                (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (137-THREONINE)
                (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (HUMAN)"/CN)
L9            1 SEA FILE=REGISTRY TAQI/CN OR "TAQI ENDONUCLEASE"/CN
L10           1 SEA FILE=HCAPLUS L5
L11         254 SEA FILE=HCAPLUS L6 OR MC4R OR MELANOCORTIN(W)4 OR MC4(W)(R OR
                RECEPTOR?)
L13        1790 SEA FILE=HCAPLUS L9 OR TAQI OR TAQ(W)I
L15           1 SEA FILE=HCAPLUS L11 AND L13
L16           0 SEA FILE=HCAPLUS L15 NOT L10


=> s l11 and (polymorph? or fat or feed or growth or food(w)(intake or consumption) or
weight(w)gain?)

        101429 POLYMORPH?
         91671 FAT
        145213 FEED
        826921 GROWTH
        192448 FOOD
         65968 INTAKE
```

```
        120892 CONSUMPTION
         16473 FOOD(W)(INTAKE OR CONSUMPTION)
         61765 WEIGHT
        111838 GAIN?
          1207 WEIGHT(W)GAIN?
L17        105 L11 AND (POLYMORPH? OR FAT OR FEED OR GROWTH OR FOOD(W)(INTAKE
               OR CONSUMPTION) OR WEIGHT(W)GAIN?)

=> s l17 and (pig? or porcine or swine or hog?)

        284053 PIG?
         31012 PORCINE
         37867 SWINE
          5351 HOG?
L18         10 L17 AND (PIG? OR PORCINE OR SWINE OR HOG?)

=> d stat que

L6           3 SEA FILE=REGISTRY ("MELANOCORTIN-4 RECEPTOR (112-METHIONINE)
                 (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (137-THREONINE)
                 (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (HUMAN)"/CN)
L11        254 SEA FILE=HCAPLUS L6 OR MC4R OR MELANOCORTIN(W)4 OR MC4(W)(R OR
               RECEPTOR?)
L17        105 SEA FILE=HCAPLUS L11 AND (POLYMORPH? OR FAT OR FEED OR GROWTH
               OR FOOD(W)(INTAKE OR CONSUMPTION) OR WEIGHT(W)GAIN?)
L18         10 SEA FILE=HCAPLUS L17 AND (PIG? OR PORCINE OR SWINE OR HOG?)


=> d ibib abs hitrn l18 1-10


L18  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:113383  HCAPLUS
DOCUMENT NUMBER:          134:202876
TITLE:                    Paraventricular hypothalamic .alpha.-melanocyte-
                          stimulating hormone and MTII reduce feeding without
                          causing aversive effects
AUTHOR(S):                Wirth, M. M.; Olszewski, P. K.; Yu, C.; Levine, A. S.;
                          Giraudo, S. Q.
CORPORATE SOURCE:         Minnesota Obesity Center, V.A. Medical Center,
                          Minneapolis, MN, 55417, USA
SOURCE:                   Peptides (N. Y., NY, U. S.) (2001), 22(1), 129-134
                          CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER:                Elsevier Science Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB    .alpha.-MSH appears to play a tonic inhibitory role in feeding and energy
      storage.  MTII, a specific synthetic MC3-R/MC4-R
      agonist, has similar effects on feeding in rats.  The current studies
      demonstrate that PVN administration of .alpha.-MSH or MTII decreases
      nocturnal and neuropeptide Y (NPY)-stimulated food
      intake without causing aversive effects.  Co-administration with
      NPY of 600 pmol .alpha.-MSH or 1 pmol MTII into the PVN caused a
      significant decrease in NPY-induced feeding.  PVN administration of MTII
      or .alpha.-MSH at doses effective to suppress feeding did not cause
      conditioned taste aversion (CTA).  ICV administration of .alpha.-MSH,
```

however, did cause weak CTA. These results indicate that the potent effects on feeding of MC3-R and **MC4-R** agonists when injected into the PVN are not due to aversive effects.

REFERENCE COUNT: 23
REFERENCE(S):
(2) Benoit, S; Journal of Neuroscience 2000, V20, P3442 HCAPLUS
(3) Brown, K; Regulatory Peptides 1998, V78, P89 HCAPLUS
(4) Cowley, M; Neuron 1999, V24, P155 HCAPLUS
(5) Curtis, K; Brain Research 1994, V663, P30 HCAPLUS
(7) Elmquist, J; Endocrinology 1997, V138, P839 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:840911 HCAPLUS
DOCUMENT NUMBER: 134:114291
TITLE: Chronic blockade of the **melanocortin 4** receptor subtype leads to obesity independently of neuropeptide Y action, with no adverse effects on the gonadotropic and somatotropic axes
AUTHOR(S): Raposinho, Paula D.; Castillo, Einar; D'Alleves, Violaine; Broqua, Pierre; Pralong, Francois P.; Aubert, Michel L.
CORPORATE SOURCE: Division of Biology of Growth and Reproduction, Department of Pediatrics, University of Geneva School of Medicine, Geneva, 1211/14, Switz.
SOURCE: Endocrinology (2000), 141(12), 4419-4427
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neuropeptide Y (NPY) is a powerful orexigenic factor, and .alpha.MSH is a melanocortin (MC) peptide that induces satiety by activating the **MC4 receptor** subtype. Genetic models with disruption of **MC4 receptor** signaling are assocd. with obesity. In the present study, a 7-day intracerebroventricular infusion to male rats of either the MC receptor antagonist SHU9119 or **porcine** NPY (10 nmol/day) was shown to strongly stimulate food and water intake and to markedly increase **fat** pad mass. Very high plasma leptin levels were found in NPY-treated rats (27.1.+-.1.8 ng/mL compared with 9.9.+-.0.9 ng/mL in SHU9119-treated animals and 2.1.+-.0.2 ng/mL in controls). As expected, NPY infusion induced hypogonadism, characterized by an impressive decrease in seminal vesicle and prostate wts. No such effects were seen with the SHU9119 infusion. Similarly, whereas the somatotropic axis of NPY-treated rats was fully inhibited, this axis was normally activated in the obese SHU9119-treated rats. Chronic infusion of SHU9119 strikingly reduced hypothalamic gene expression for NPY (65.2.+-.3.6% of controls), whereas gene expression for POMC was increased (170.+-.19%). NPY infusion decreased hypothalamic gene expression for both POMC and NPY (70.+-.9% and 75.4.+-.9.5%, resp.). In summary, blockade of the **MC4 receptor** subtype by SHU9119 was able to generate an obesity syndrome with no apparent side-effects on the reproductive and somatotropic axes. In this situation, it is unlikely that hyperphagia was driven by increased NPY release, because hypothalamic NPY gene expression

was markedly reduced, suggesting that hyperphagia mainly resulted from loss of the satiety signal driven by MC peptides. NPY infusion produced hypogonadism and hyposomatotropism in the face of markedly elevated plasma leptin levels and an important redn. in hypothalamic POMC synthesis. In this situation NPY probably acted both by exacerbating **food intake** through Y receptors and by reducing the satiety signal driven by MC peptides.

REFERENCE COUNT: 67
REFERENCE(S):
(1) Aubert, M; Mol Cell Endocrinol 1998, V140, P107 HCAPLUS
(2) Brady, L; Neuroendocrinology 1990, V52, P441 HCAPLUS
(3) Breier, B; J Endocrinol 1991, V128, P347 HCAPLUS
(5) Catzeflis, C; Endocrinology 1993, V132, P224 HCAPLUS
(6) Chehab, F; Nat Genet 1996, V12, P318 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:117783 HCAPLUS
DOCUMENT NUMBER: 133:115728
TITLE: A missense variant of the **porcine melanocortin-4** receptor (**MC4R**) gene is associated with fatness, **growth**, and **feed** intake traits
AUTHOR(S): Kim, Kwan Suk; Larsen, Niels; Short, Tom; Plastow, Graham; Rothschild, Max F.
CORPORATE SOURCE: Department of Animal Science, Iowa State University, Ames, IA, 50011, USA
SOURCE: Mamm. Genome (2000), 11(2), 131-135
CODEN: MAMGEC; ISSN: 0938-8990
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

not prior

AB Our knowledge of the genetic factors affecting obesity is increasing, but information about the individual gene effects remains limited in humans as well as in animal models. The **melanocortin-4** receptor gene (**MC4R**) has been implicated in the regulation of feeding behavior and body wt. in humans and mice. We have studied **MC4R** as a candidate gene for the control of economically important **growth** and performance traits in the **pig**. A missense mutation was identified in a region highly conserved among melanocortin receptor (MCR) genes. To det. whether there was an assocn. of this **MC4R polymorphism** with phenotypic variation, we tested the mutation in a large no. of individual animals from several different **pig** lines. Analyses of **growth** and performance test records showed significant assocns. of **MC4R** genotypes with backfat and **growth** rate in a no. of lines as well as **feed** intake overall. It is probable that the variant amino acid residue of the **MC4R** mutation (or a closely linked mutation) causes a significant change of the **MC4R** function. These results support the functional significance of a **pig MC4R** missense mutation and suggest that comparative genomics based on model species may be equally important for application to farm animals as they are for human medicine.

REFERENCE COUNT: 36

REFERENCE(S):
(1) Andersson, L; Ann Med 1996, V28, P5 HCAPLUS
(2) Andersson, L; Science 1994, V263, P1771 HCAPLUS
(3) Casas-Carrillo, E; J Anim Sci 1997, V75, P2047 HCAPLUS
(5) Flier, J; Cell 1998, V92, P437 HCAPLUS
(6) Frandberg, P; Biochem Biophys Res Commun 1997, V236, P489 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:98833 HCAPLUS
DOCUMENT NUMBER: 132:162049
TITLE: **Porcine melanocortin-4** receptor gene and use as a genetic marker for **fat** content, **weight gain**, and/or **feed** consumption of animals
INVENTOR(S): Rothschild, Max F.; Larson, Niels J.; Kim, Kwan Suk
PATENT ASSIGNEE(S): Iowa State University Research Foundation, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

priority doc

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006777	A2	20000210	WO 1999-US16862	19990726
WO 2000006777	A3	20000511		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9952301	A1	20000221	AU 1999-52301	19990726
PRIORITY APPLN. INFO.:			US 1998-94287	19980727
			US 1999-116186	19990115
			WO 1999-US16862	19990726

AB Genetic markers in the **porcine melanocortin-4** receptor (**MC4R**) gene are disclosed which are assocd. with **fat** content, **growth** rate, and **feed** consumption. Further, novel sequence data from regions of the gene are disclosed which may be used in a PCR test to screen for the presence of the marker. The genetic marker may be used to screen animals for breeding purposes which have the desired traits regarding **fat** content, **growth** rate, and **feed** consumption. The screening methods disclosed in the invention involve analyzing animals for a **polymorphism** in the **MC4R** gene, and test kits which take advantage of the PCR test are also disclosed.

L18 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:795994 HCAPLUS

DOCUMENT NUMBER: 132:31744
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
SOURCE: PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	
GB 1998-12099	19980606
GB 1998-13291	19980620
GB 1998-13611	19980624
GB 1998-13835	19980627
GB 1998-14110	19980701
GB 1998-14580	19980707
GB 1998-15438	19980716
GB 1998-15574	19980718
GB 1998-15576	19980718
GB 1998-16085	19980724
GB 1998-16086	19980724
GB 1998-16921	19980805
GB 1998-17097	19980807
GB 1998-17200	19980808
GB 1998-17632	19980814
GB 1998-17943	19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that **polymorphisms** within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and **polymorphisms**) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a

design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L18 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:795993 HCAPLUS
DOCUMENT NUMBER: 132:31743
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941586	A1	19991230	AU 1999-41586	19990604
AU 9941587	A1	19991230	AU 1999-41587	19990604
GB 2339200	A1	20000119	GB 1999-12914	19990604
EP 1084273	A1	20010321	EP 1999-925207	19990604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

GB 1998-12098	19980606
GB 1998-28289	19981223
GB 1998-16086	19980724
GB 1998-16921	19980805
GB 1998-17097	19980807
GB 1998-17200	19980808
GB 1998-17632	19980814
GB 1998-17943	19980819
WO 1999-GB1779	19990604

AB There is considerable evidence that significant factor underlying the

individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that **polymorphisms** within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and **polymorphisms**) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L18 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:764612 HCAPLUS
DOCUMENT NUMBER: 132:220252
TITLE: Agouti antagonism of melanocortin receptors: central and peripheral effects on obesity and diabetes
AUTHOR(S): Mynatt, Randall L.
CORPORATE SOURCE: Pennington Biomedical Research Center, Baton Rouge, LA, 70808, USA
SOURCE: Pennington Cent. Nutr. Ser. (1999), 9(Nutrition, Genetics, and Obesity), 306-319
CODEN: PCNSEW; ISSN: 1063-8822
PUBLISHER: Louisiana State University Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 41 refs. Agouti was the first of several recently cloned genes in which mutations lead to obesity in mice. Agouti protein normally functions as a secreted protein acting in a paracrine manner to regulate coat color in mammals. In melanocytes, agouti antagonizes the binding of .alpha.-MSH (.alpha.-MSH) to melanocortin receptor-1 (MC1-R), causing a switch from synthesis of black **pigments** to yellow **pigment**. Several dominant mutations at agouti cause the ectopic expression of wild type agouti resulting in a condition similar to adult-onset obesity and non-insulin-dependent diabetes mellitus. Melanocortin receptors are a group of five membrane spanning proteins coupled to G-proteins that activate adenylate cyclase in many tissues. Agouti protein is thought to mimic the natural antagonism of melanocortin receptors to cause obesity. In addn. to its role in melanogenesis, .alpha.-MSH is also a potent inhibitor of **food intake**. Targeted mutagenesis of **MC4-R** recapitulates several of the characteristic features of agouti-induced obesity. The endogenous antagonist of **MC4-R** appears to be an agouti-related protein AGRP which is expressed in the brain and adrenals. Transgenic mice that over express AGRP also become obese. A current model is that agonism, via .alpha.-MSH, of **MC4-R** causes a tonic inhibition of **food intake** that is blocked in the presence of AGRP. Therefore it seems that the primary mechanism of agouti-induced obesity in mice is to mimic the normal antagonism of brain melanocortin receptors. However, the specific area of the brain and/or cell types being influenced by ARGP and melanocortins has not been

confirmed.
REFERENCE COUNT: 41
REFERENCE(S):
(1) Buffey, J; Pigment Cell Res 1993, V6(6), P385 HCAPLUS
(2) Bultman, S; Cell 1992, V71(7), P1195 HCAPLUS
(3) Chen, W; Cell 1997, V91, P789 HCAPLUS
(4) Comuzzie, A; Nature Genet 1997, V15(3), P273 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:246481 HCAPLUS
DOCUMENT NUMBER: 131:86044
TITLE: **Melanocortin-4** receptor: a novel signalling pathway involved in body weight regulation
AUTHOR(S): Fisher, S. L.; Yagaloff, K. A.; Burn, P.
CORPORATE SOURCE: Department of Metabolic Diseases, Hoffmann LaRoche, Nutley, NJ, 07110, USA
SOURCE: Int. J. Obes. (1999), 23(Suppl. 1), 54-58
CODEN: IJOBDP; ISSN: 0307-0565
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 37 refs. For many years, genetically obese mouse strains have provided models for human obesity. The Avy/-agouti mouse, one of the oldest obese mouse models, is characterized by maturity-onset obesity and diabetes as a result of ectopic expression of the secreted protein hormone, agouti protein. Agouti protein is normally expressed in hair follicles to regulate **pigmentation** through antagonism of the melanocortin-1 receptor, but in-vitro studies have demonstrated that the hormone also has potent antagonist activity for the **melanocortin -4** receptor (**MC4-R**). Subsequent development of the **MC4-R** knockout mouse model demonstrated that **MC4-R** plays a role in wt. homeostasis as these mice recapitulated the metabolic defects of the agouti mouse. Further evidence for this hypothesis was obtained from pharmacol. studies utilizing peptides with **MC4-R** agonist activity, that inhibited **food intake** (when administered intracerebrally). Addnl. studies with peptide antagonists have now implicated the **MC4-R** in the leptin signaling pathway. Finally, evidence that the **MC4-R** may play a role in human obesity has been obtained from the identification of a dysfunctional variant of the receptor in genetically obese subjects.
REFERENCE COUNT: 37
REFERENCE(S):
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(2) Barsh, G; Trends Gene 1996, V12, P299 HCAPLUS
(3) Boston, B; Science 1997, V278, P1641 HCAPLUS
(5) Bultman, S; Cell 1992, V71, P1195 HCAPLUS
(6) Campfield, L; Endocrin Metab 1997, V4, P81 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:763259 HCAPLUS
DOCUMENT NUMBER: 130:134078
TITLE: Discovery of a novel superpotent and selective

melanocortin-4 receptor antagonist (HS024): evaluation in vitro and in vivo

AUTHOR(S): Kask, Ants; Mutulis, Felikss; Muceniece, Ruta; Pahkla, Rein; Mutule, Ilze; Wikberg, Jarl E. S.; Rago, Lembit; Schioth, Helgi B.

CORPORATE SOURCE: Department of Pharmacology, University of Tartu, Tartu, 50090, Estonia

SOURCE: Endocrinology (1998), 139(12), 5006-5014
CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several novel cyclic MSH analogs were synthesized, and their binding properties were tested on cells transiently expressing the human melanocortin-1 (MC1), MC3, MC4, and MC5 receptors. We discovered a novel substance (HS024) that showed about 20-fold selectivity and very high affinity (Ki = 0.29 nM) for the **MC4 receptor**. HS024 (cyclic [AcCys3,Nle4,Arg5,D-Nal7,Cys-NH211].alpha.-MSH-(3-11)) has a 29-membered atom ring structure that includes an Arg in position 5. HS024 was found to antagonize an .alpha.MSH-induced cAMP response in cells expressing the human MC1, MC3, MC4, and MC5 receptor DNAs. HS024 also caused a dose-dependent increase in **food intake**, with a max. response (4-fold increase) at a 1-nmol dose injected intracerebroventricularly in free feeding rats. We also tested SHU9119, a previously described nonselective MC receptor antagonist, and found HS024 and SHU9119 to have similar potencies for increasing **food intake**, although SHU9119 appeared to induce more serious side-effects. HS024 increased the **food intake** of free feeding rats to levels comparable to those in food-deprived rats, indicating that blockade of the **MC4 receptor** is a highly effective way to increase feeding. Moreover, we tested the effects of intracerebroventricular injections of HS024 in elevated plus-maze and open-field expts. on rats. In these tests, HS024 did not appear to affect emotionality or locomotor activity, suggesting that the **MC4 receptor** does not mediate the anxiogenic-like and locomotor effects related to the melanocortic peptides.

REFERENCE COUNT: 49
REFERENCE(S):
(1) Al-Obeidi, F; J Med Chem 1989, V32, P2555 HCAPLUS
(2) Biro, E; Neuroendocrinology 1993, V57, P340 HCAPLUS
(4) Chen, W; Cell 1997, V91, P789 HCAPLUS
(5) Chhajlani, V; Biochem Biophys Res Commun 1993, V195, P866 HCAPLUS
(6) Chhajlani, V; FEBS Lett 1992, V309, P417 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:564854 HCAPLUS
DOCUMENT NUMBER: 129:274097

TITLE: Severe early-onset obesity, adrenal insufficiency and red hair **pigmentation** caused by POMC mutations in humans

AUTHOR(S): Krude, Heiko; Biebermann, heike; Luck, Werner; Horn, Rudiger; Brabant, Georg; Gruters, Annette

CORPORATE SOURCE: Dep. Pediatrics, Humboldt-Univ., Berlin, Germany

SOURCE: Nat. Genet. (1998), 19(2), 155-157

CODEN: NGENEC; ISSN: 1061-4036
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sequential cleavage of the precursor protein pre-pro-opiomelanocortin (POMC) generates the melanocortin peptides ACTH (ACTH), melanocyte-stimulating hormones (MSH) .alpha., .beta. and .gamma. as well as the opioid-receptor ligand .beta.-endorphin. While a few cases of isolated ACTH deficiency have been reported (OMIM 201400), an inherited POMC defect has not been described so far. Recent studies in animal models elucidated a central role of .alpha.-MSH in the regulation of **food intake** by activation of the brain **melanocortin-4**-receptor (**MC4-R**; refs 3-5) and the linkage of human obesity to chromosome 2 in close proximity to the POMC locus, led to the proposal of an assocn. of POMC with human obesity. The dual role of .alpha.-MSH in regulating **food intake** and influencing hair **pigmentation** predicts that the phenotype assocd. with a defect in POMC function would include obesity, alteration in **pigmentation** and ACTH deficiency. The observation of these symptoms in two probands promoted us to search for mutations within their POMC genes. Patient 1 was found to be a compd. heterozygote for two mutations in exon 3 (G7013T, C7133.DELTA.) which interfere with appropriate synthesis of ACTH and .alpha.-MSH. Patient 2 was homozygous for a mutation in exon 2 (C3804A) which abolishes POMC translation. These findings represent the first examples of a genetic defect within the POMC gene and define a new monogenic endocrine disorder resulting in early-onset obesity, adrenal insufficiency and red hair **pigmentation**.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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L6 3 SEA FILE=REGISTRY ("MELANOCORTIN-4 RECEPTOR (112-METHIONINE) (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (137-THREONINE) (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (HUMAN)"/CN)

L11 254 SEA FILE=HCAPLUS L6 OR MC4R OR MELANOCORTIN(W)4 OR MC4(W)(R OR RECEPTOR?)

L19 94 SEA FILE=HCAPLUS L11 (L) (POLYMORPH? OR FAT OR FEED OR GROWTH OR FOOD(W)(INTAKE OR CONSUMPTION) OR WEIGHT(W)GAIN?)

L20 47 SEA FILE=HCAPLUS (GENE? OR DNA OR NUCLEIC) AND L19

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L20 ANSWER 1 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:207384 HCAPLUS
TITLE: Agouti-related protein functions as an inverse agonist at a constitutively active brain melanocortin-4 receptor
AUTHOR(S): Haskell-Luevano, C.; Monck, E. K.
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, 32610-0485, Gainesville, FL, USA

SOURCE: Regul. Pept. (2001), 99(1), 1-7
CODEN: REPPDY; ISSN: 0167-0115
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Agouti-related protein (AGRP) is one of two naturally occurring antagonists of G-Protein coupled receptors (GPCRs) identified to date, and has been physiol. implicated in regulating **food intake**, body wt., and energy homeostasis. AGRP has been identified in vitro, as competitively antagonizing the brain **melanocortin-4** (**MC4R**) and melanocortin-3 (MC3R) receptors, and when over expressed in transgenic mice, results in an obese phenotype. Emerging data propose that AGRP has addnl. targets in the hypothalamus and/or physiol. functions via a mechanism in addn. to competitive antagonism of .alpha.-MSH at the brain melanocortin receptors. We report data herein supporting an alternative mechanism for AGRP involvement in feeding behavior. A constitutively active **MC4R** has been **generated** which possess EC50 values for melanocortin agonists (.alpha.-MSH, NDP-MSH, and MTII) and a pA2 value for the synthetic peptide antagonist SHU9119 identical to the wildtype receptor, but increases basal activity to 50% maximal response. AGRP possesses inverse agonist activity at this constitutively active **MC4R**. These data support the hypothesis for an addnl. physiol. mechanism for AGRP action in feeding behavior and energy homeostasis.

L20 ANSWER 2 OF 47 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:202139 HCAPLUS
TITLE: Computer aid drug design of melanocortin receptor MC4 agonist as a promising cure of obesity
AUTHOR(S): Gao, Yinghong; Goodfellow, Val
CORPORATE SOURCE: Department of Medicinal Chemistry, Neurocrine Biosciences Incorporation, San Diego, CA, 92121, USA
SOURCE: Abstr. Pap. - Am. Chem. Soc. (2001), 221st, MEDI-235
CODEN: ACSRAL; ISSN: 0065-7727
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English

AB Obesity has been one of the leading causes of life threatening diseases. **Genetic** and pharmacol. studies have led to the discovery of the pivotal roles of **melanocortin-4** receptor in the regulation of **food intake** behavior. Weakly active small mol. **MC4R** agonists have been identified using HTS. Multi-channel computational approach was then applied in lead exploratory and optimization. Eigenvalue based low dimensional BCUT chem. space of **MC4R** agonist was defined and pharmacophore models are developed. Similarity search and computer aid mol. design led to the discovery of new leads. Hypothesis are redefined and used for virtual screening to enrich the hit rate. More preliminary results from virtual screening will be discussed.

L20 ANSWER 3 OF 47 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:89290 HCAPLUS
TITLE: Monogenic forms of obesity: from mice to human
AUTHOR(S): Clement, K.
CORPORATE SOURCE: Beckman Center, HHMI/Stanford University, Stanford, CA, USA

SOURCE: Ann. Endocrinol. (2000), 61(6, Suppl.), 39-49
CODEN: ANENAG; ISSN: 0003-4266
PUBLISHER: Masson Editeur
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cloning of five rodent obesity **genes** has constituted a major advance in our understanding of body wt. homeostasis. Breakthroughs in human mol. **genetics** have identified mutations disrupting either rodent homolog/analog **genes** or **genes** involved in the same pathways in obese patients. Three rare cases of human morbid obesity of early onset assocd. with hypogodatropic hypogodanism are due to mutations in the leptin and the leptin receptor **genes**. These studies have confirmed that leptin plays not only a crucial role in the control of body wt. in the human but also in several endocrine functions. Other Human obesity syndromes are linked to mutations in the **genes** encoding brain-expressed targets of leptin, particularly some key components of the melanocortin system. Patients compd. heterozygous for mutations in the POMC **gene** display severe obesity of early onset, congenital adrenal insufficiency and red hair. Another **genetic** cause of obesity is due to mutation in the Proconvertase **gene** (PC1), the enzyme required for the cleavage of POMC into ACTH and alpha MSH, and also of Proinsulin to insulin. The subject compd. heterozygous for the PC1 mutation displays besides obesity, a partial ACTH deficiency, elevated POMC and late post absorptive hypoglycemia due to the accumulation of high pro-insulinemia. Contrasting largely with these rare syndromic forms of obesity, several mutations located in the **melanocortin 4** receptor **gene** have been showed to cause an early onset dominant form of obesity with no other assocd. abnormalities indifferent populations. These mutations in **MC4-R** could represent a <<frequent>> cause of common monogenic forms of obesity in human. More **generally**, these researches into human obesity have opened new exciting understandings in some of the pathways regulating body **fat** mass.

REFERENCE COUNT: 35
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 47 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:42062 HCAPLUS
DOCUMENT NUMBER: 134:50908
TITLE: New development in the drug therapy of obesity
AUTHOR(S): Namai, Kazuyuki; Kanazawa, Yasunori
CORPORATE SOURCE: Omiya Med. Cent., Jichi Med. Sch., Japan
SOURCE: Horumon to Rinsho (2000), 48(12), 1145-1151
CODEN: HORIAE; ISSN: 0045-7167
PUBLISHER: Igaku no Sekaisha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 24 refs., on the strategies for drug therapy of obesity, mechanisms of appetite-suppressing actions of leptin and leptin analogs, obesity caused by mutations in **MC4 receptor**

gene, action mechanisms of appetite depressants (catecholaminergic agents, serotonergic agents, and sibutramine), effects of a **fat** absorption inhibitor (a lipase inhibitor, orlistat), and thermogenesis stimulation through .beta.3-adrenergic receptor.

L20 ANSWER 5 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:896080 HCAPLUS
TITLE: Candidate **gene** polymorphisms in eating disorders
AUTHOR(S): Hinney, A.; Remschmidt, H.; Hebebrand, J.
CORPORATE SOURCE: Clinical Research Group, Department of Child and Adolescent Psychiatry, Philipps-University of Marburg, Marburg, D-35033, Germany
SOURCE: Eur. J. Pharmacol. (2000), 410(2/3), 147-159
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Anorexia nervosa and bulimia nervosa are complex disorders characterized by disordered eating behavior. Attitudes towards wt. and shape as well as the perception of body shape are disturbed. A substantial **genetic** influence on these disorders has been suggested by formal **genetic** studies. Obsessive-compulsive behavior, perfectionism and anxious personality traits seem to occur premorbidly in several patients. Disturbances of neurotransmitter, neuropeptide and neuroendocrine systems have been reported in acutely ill and followed-up patients. Hence, these systems might be involved in the etiol. of these eating disorders. **Genetic** studies on candidate **genes** have mainly focussed on the serotonergic system and on **genes** involved in body wt. regulation. Up to now, **polymorphisms** and variations in various **genes** (e.g. **genes** for 5-HT receptors, leptin **gene**, melanocortin **MC4 receptor gene**) have been assessed for assocn. and transmission disequil. pertaining to anorexia nervosa and/or bulimia nervosa. Most of the studies yielded neg. results. Four studies of a **polymorphism** (-1438 G/A) within the promoter of the 5-HT2A **gene** (5-HT2A) revealed an assocn. of the A-allele to anorexia nervosa. However, three studies could not confirm this result. Furthermore, a meta-anal. did not support the pos. assocn. Currently, combined efforts within the European Union will answer the question of whether or not the A-allele is involved in the predisposition to anorexia nervosa. A transmission disequil. test is being performed in about 300 trios consisting of a patient with anorexia nervosa and both parents. As candidate **gene** approaches did not unequivocally identify susceptibility **genes** (alleles) for anorexia nervosa or bulimia nervosa, systematic model-free genome-wide screenings should also be performed in order to identify currently unknown **genes** involved in eating disorders. This kind of approach has already been initiated for anorexia nervosa. **Genetic** research on eating disorders will hopefully lead to new pharmacol. treatment strategies.
REFERENCE COUNT: 136
REFERENCE(S):
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(2) Akabayashi, A; Mol Cell Neurosci 1994, V5, P210 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:840911 HCAPLUS
DOCUMENT NUMBER: 134:114291
TITLE: Chronic blockade of the melanocortin 4 receptor subtype leads to obesity independently of neuropeptide Y action, with no adverse effects on the gonadotropic and somatotropic axes
AUTHOR(S): Raposinho, Paula D.; Castillo, Einar; D'Alleves, Violaine; Broqua, Pierre; Pralong, Francois P.; Aubert, Michel L.
CORPORATE SOURCE: Division of Biology of Growth and Reproduction, Department of Pediatrics, University of Geneva School of Medicine, Geneva, 1211/14, Switz.
SOURCE: Endocrinology (2000), 141(12), 4419-4427
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neuropeptide Y (NPY) is a powerful orexigenic factor, and .alpha.MSH is a melanocortin (MC) peptide that induces satiety by activating the **MC4 receptor** subtype. **Genetic** models with disruption of **MC4 receptor** signaling are assocd. with obesity. In the present study, a 7-day intracerebroventricular infusion to male rats of either the MC receptor antagonist SHU9119 or porcine NPY (10 nmol/day) was shown to strongly stimulate food and water intake and to markedly increase **fat** pad mass. Very high plasma leptin levels were found in NPY-treated rats (27.1.+-.1.8 ng/mL compared with 9.9.+-.0.9 ng/mL in SHU9119-treated animals and 2.1.+-.0.2 ng/mL in controls). As expected, NPY infusion induced hypogonadism, characterized by an impressive decrease in seminal vesicle and prostate wts. No such effects were seen with the SHU9119 infusion. Similarly, whereas the somatotropic axis of NPY-treated rats was fully inhibited, this axis was normally activated in the obese SHU9119-treated rats. Chronic infusion of SHU9119 strikingly reduced hypothalamic **gene** expression for NPY (65.2.+-.3.6% of controls), whereas **gene** expression for POMC was increased (170.+-.19%). NPY infusion decreased hypothalamic **gene** expression for both POMC and NPY (70.+-.9% and 75.4.+-.9.5%, resp.). In summary, blockade of the **MC4 receptor** subtype by SHU9119 was able to **generate** an obesity syndrome with no apparent side-effects on the reproductive and somatotropic axes. In this situation, it is unlikely that hyperphagia was driven by increased NPY release, because hypothalamic NPY **gene** expression was markedly reduced, suggesting that hyperphagia mainly resulted from loss of the satiety signal driven by MC peptides. NPY infusion produced hypogonadism and hyposomatotropism in the face of markedly elevated plasma leptin levels and an important redn. in hypothalamic POMC synthesis. In this situation NPY probably acted both by exacerbating **food intake** through Y receptors and by reducing the satiety signal driven by MC peptides.
REFERENCE COUNT: 67
REFERENCE(S): (1) Aubert, M; Mol Cell Endocrinol 1998, V140, P107 HCAPLUS

(2) Brady, L; Neuroendocrinology 1990, V52, P441 HCAPLUS
(3) Breier, B; J Endocrinol 1991, V128, P347 HCAPLUS
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(6) Chehab, F; Nat Genet 1996, V12, P318 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:840903 HCAPLUS
DOCUMENT NUMBER: 134:51648
TITLE: Photoperiod regulates growth, puberty and hypothalamic neuropeptide and receptor **gene** expression in female Siberian hamsters
AUTHOR(S): Adam, Clare L.; Moar, Kim M.; Logie, Tracy J.; Ross, Alexander W.; Barrett, Perry; Morgan, Peter J.; Mercer, Julian G.
CORPORATE SOURCE: Molecular Neuroendocrinology Group, Aberdeen Centre for Energy Regulation and Obesity, Rowett Research Institute, Aberdeen, AB21 9SB, UK
SOURCE: Endocrinology (2000), 141(12), 4349-4356
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In seasonal mammals, both the growth and reproductive axes are regulated by photoperiod. Female Siberian hamsters were kept, for up to 12 wk, in long-day (LD) or short-day (SD) photoperiod, from weaning at 3 wk of age (Exp 1). LD hamsters had characteristically faster growth and higher asymptotic body wt., adiposity, and leptin **gene** expression in adipose tissue. Only LD females attained puberty. **Gene** expression in the hypothalamic arcuate nucleus for leptin receptor (OB-Rb), POMC, and melanocortin 3-receptor (MC3-R) was higher in LD but did not change from weaning levels in SD. In contrast, **gene** expression in the arcuate nucleus for cocaine and amphetamine-regulated transcript (CART) was higher in SD than LD, a difference that was apparent at 2 wk post weaning. Transfer of SD females to LD at 15 wk post weaning (Exp 2) increased body wt., leptin signal, and **gene** expression for POMC but failed to induce normal puberty onset or to increase **gene** expression for OB-Rb and MC3-R. Therefore, photoperiodic regulation of puberty may be modulated by age, by photoperiodic history, and by changes in leptin signaling and the activity of the leptin-sensitive hypothalamic melanocortin system (POMC, MC3-R). A role for CART in photoperiodic regulation of growth is suggested, because the changes in CART **gene** expression preceded significant divergence of growth trajectories in the opposite photoperiods.
REFERENCE COUNT: 34
REFERENCE(S):

(1) Cheung, C; Endocrinology 1997, V138, P4489 HCAPLUS
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(4) Ebling, F; Gen Comp Endocrinol 1994, V95, P475 HCAPLUS
(5) Elias, C; Neuron 1998, V21, P1375 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:720147 HCAPLUS
DOCUMENT NUMBER: 133:329703
TITLE: Role of melanocortins in the central control of feeding
AUTHOR(S): Vergoni, A. V.; Bertolini, A.
CORPORATE SOURCE: Department of Biomedical Sciences, Section of Pharmacology, University of Modena and Reggio Emilia, Modena, 41100, Italy
SOURCE: Eur. J. Pharmacol. (2000), 405(1-3), 25-32
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 82 refs. The injection of a melanocortin peptide or of melanocortin peptide analogs into the cerebrospinal fluid or into the ventromedial hypothalamus in nanomolar or sub-nanomolar doses induces a long-lasting inhibition of **food intake**. The effect keeps significant for up to 9 h and has been obsd. in all animal species so far tested, the most susceptible being the rabbit. The anorectic effect of these peptides is a primary one, not secondary to the shift towards other components of the complex melanocortin-induced behavioral syndrome, in particular grooming. The site of action is in the brain, and the effect is not adrenal-mediated because it is fully exhibited also by adrenalectomized animals. It is a very strong effect, because the degree of feeding inhibition is not reduced in conditions of hunger, either induced by 24 h starvation, or by insulin-induced hypoglycemia, or by stimulation of .gamma.-aminobutyric acid (GABA), noradrenergic or opioid systems. The microstructural anal. of feeding behavior suggests that melanocortins act as satiety-inducing agents, because they do not significantly modify the latencies to start eating, but shorten the latencies to stop eating. The mechanism of action involves the activation of melanocortin **MC4 receptors**, because selective melanocortin **MC4 receptor** antagonists inhibit the anorectic effect of melanocortins, while inducing per se a strong stimulation of **food intake** and a significant increase in body wt. Melanocortins seem to play an important role in stress-induced anorexia, because such condition, in rats, is significantly attenuated by the blockage of melanocortin **MC4 receptors** ; such a role is not secondary to an increased release of corticotropin-releasing factor (CRF), because, the CRF-induced anorexia is not affected at all by the blockage of melanocortin **MC4 receptors**. The physiol. meaning of the feeding inhibitory effect of melanocortins, and, by consequence, the physiol. role of melanocortins in the complex machinery responsible for body wt. homeostasis, is testified by the hyperphagia/obesity syndromes caused by mutations in the pro-opiomelanocortin (POMC) **gene**, or in the melanocortin **MC4 receptor gene**, or in the agouti locus. Finally, recent evidences suggest that melanocortins could be involved in mediating the effects of leptin, and in controlling the expression of neuropeptide Y (NPY).

REFERENCE COUNT: 82
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 9 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:690041 HCAPLUS
DOCUMENT NUMBER: 133:344856
TITLE: Disproportionate inhibition of feeding in Ay mice by certain stressors: a cautionary note
AUTHOR(S): De Souza, Jose; Butler, Andrew A.; Cone, Roger D.
CORPORATE SOURCE: Vollum Institute, Oregon Health Sciences University, Portland, OR, 97201, USA
SOURCE: Neuroendocrinology (2000), 72(2), 126-132
CODEN: NUNDAJ; ISSN: 0028-3835
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A study of the effects of insulin-induced hypoglycemia in the obese yellow agouti Ay mouse was initiated to test the hypothesis that the central melanocortin pathways are required for a normal sympathetic response to hypoglycemia. An exptl. protocol was performed in which young nonobese male mice were isolated and fasted beginning on day 1, then tested for glucose responses to insulin-induced hypoglycemia on day 2. Normal mice demonstrated the expected glucose rebound to hypoglycemia, exceeding baseline glucose levels by 2-3 times as a consequence of increased gluconeogenesis and glycogenolysis before returning to baseline levels. Ay animals lacked the rebound, exhibiting instead a gradual restoration of baseline glucose levels. The results suggested a defective sympathetic response to hypoglycemia in the Ay mouse. However, a more detailed anal. demonstrated that the lack of a hyperglycemic rebound was due to an acute inhibition of feeding specifically in the Ay mouse, which resulted not from the hypoglycemia stressor, but rather from the stress of isolation. Handling and i.p. administration of saline also specifically inhibited **food intake** in the Ay but not the wild-type mouse, while restraint stress had an equiv. inhibitory effect on **food intake** on wild-type and Ay mice. Since the Ay mouse has defective hypothalamic **melanocortin-4** receptor (**MC4-R**) signaling, these data imply that the central melanocortin pathway is necessary for regulating the effects of stress on feeding behavior. Furthermore, these data demonstrate the need for exercising extreme caution in designing expts. to analyze feeding behavior and metab. in **genetic** or pharmacol. models involving perturbation of the melanocortin system.
REFERENCE COUNT: 17
REFERENCE(S): (1) Boston, B; Science 1997, V278, P1641 HCAPLUS
(2) Calogero, A; J Clin Invest 1988, V82, P767 HCAPLUS
(3) Graham, M; Nat Genet 1997, V17, P273 HCAPLUS
(4) Haynes, W; Hypertension 1999, V33, P542 HCAPLUS
(5) Hinney, A; J Clin Endocrinol Metab 1999, V84, P1483 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 10 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:646802 HCAPLUS
DOCUMENT NUMBER: 133:332799

TITLE: Inactivation of the mouse melanocortin-3 receptor results in increased fat mass and reduced lean body mass
AUTHOR(S): Chen, Airu S.; Marsh, Donald J.; Trumbauer, Myrna E.; Frazier, Easter G.; Guan, Xiao-Ming; Yu, Hong; Rosenblum, Charles I.; Vongs, Aurawan; Feng, Yue; Cao, Linhai; Metżger, Joseph M.; Strack, Alison M.; Camacho, Ramon E.; Mellin, Theodore N.; Nunes, Christian N.; Min, William; Fisher, Jill; Gopal-Truter, Shobhna; MacIntyre, D. Euan; Chen, Howard Y.; Van der Ploeg, Lex H. T.
CORPORATE SOURCE: Department of Obesity Research, Merck Research Laboratories, Rahway, NJ, USA
SOURCE: Nat. Genet. (2000), 26(1), 97-102
CODEN: NGENEC; ISSN: 1061-4036
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Genetic** and pharmacol. studies have defined a role for the **melanocortin-4** receptor (**Mc4r**) in the regulation of energy homeostasis. The physiol. function of Mc3r, a melanocortin receptor expressed at high levels in the hypothalamus, has remained unknown. We evaluated the potential role of Mc3r in energy homeostasis by studying Mc3r-deficient (Mc3r-/-) mice and compared the functions of Mc3r and **Mc4r** in mice deficient for both **genes**. The 4-6-mo Mc3r-/- mice have increased **fat** mass, reduced lean mass and higher **feed** efficiency than wild-type littermates, despite being hypophagic and maintaining normal metabolic rates. **Feed** efficiency is the ratio of wt. gain to **food intake**. Consistent with increased **fat** mass, Mc3r-/- mice are hyperleptinemic and male Mc3r-/- mice develop mild hyperinsulinemia. Mc3r-/- mice did not have significantly altered corticosterone or total thyroxine (T4) levels. Mice lacking both Mc3r and **Mc4r** become significantly heavier than **Mc4r**-/- mice. We conclude that Mc3r and **Mc4r** serve non-redundant roles in the regulation of energy homeostasis.
REFERENCE COUNT: 30
REFERENCE(S): (2) Chagnon, Y; Mol Med 1997, V3, P663 HCAPLUS
(4) Chhajlani, V; Biochem Mol Biol Int 1996, V38, P73 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 11 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:603863 HCAPLUS
DOCUMENT NUMBER: 133:279949
TITLE: A unique metabolic syndrome causes obesity in the melanocortin-3 receptor-deficient mouse
AUTHOR(S): Butler, Andrew A.; Kesterson, Robert A.; Khong, Kathy; Cullen, Mary Jane; Pelleymounter, Mary Ann; Dekoning, Jenefer; Baetscher, Manfred; Cone, Roger D.
CORPORATE SOURCE: Vollum Institute, OHSU, Portland, OR, 97201-3098, USA
SOURCE: Endocrinology (2000), 141(9), 3518-3521
CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The central melanocortin system is crit. for the long term regulation of energy homeostasis. Null mutations of the **melanocortin-4** receptor (**MC4-R**) are assocd. with hyperphagia, obesity, and accelerated longitudinal **growth** in mice and humans. However, little is known about the function of another central melanocortin receptor, the MC3-R. To assess the role of the MC3-R in energy homeostasis, the majority of the mc3r coding sequence was deleted from the mouse genome. In contrast to the **MC4-R** knockout, which exhibits increased **food intake**, increased somatic **growth**, and defects in metab., mc3r-/- mice exhibit an exclusively metabolic syndrome. Homozygous null mc3r mice, while not significantly overweight, exhibit an approx. 50% to 60% increase in adipose mass. Mc3r-/- mice also exhibit an unusual increase in RQ when transferred onto high **fat** chow, suggesting a reduced ratio of **fat**/carbohydrate oxidn. Furthermore, male mc3r-/- mice also exhibit an approx. 50% redn. in locomotory behavior on the running wheel, suggesting reduced energy expenditure.
REFERENCE COUNT: 23
REFERENCE(S): (2) Bultman, S; Cell 1992, V71, P1195 HCAPLUS
(3) Chiang, L; Methods in Molecular Biology 1996, V57, P311 HCAPLUS
(4) Cone, R; Trends in Endocrinol and Metab 1999, V10, P211 HCAPLUS
(5) Cowley, M; Neuron 1999, V24, P155 HCAPLUS
(6) Dinulescu, D; Proc Natl Acad Sci USA 1998, V95, P12707 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 12 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:603811 HCAPLUS
DOCUMENT NUMBER: 133:233103
TITLE: The central melanocortin system can directly regulate serum insulin levels
AUTHOR(S): Fan, Wei; Dinulescu, Daniela M.; Butler, Andrew A.; Zhou, Jeanie; Marks, Daniel L.; Cone, Roger D.
CORPORATE SOURCE: The Vollum Institute, Oregon Health Sciences University, Portland, OR, 97201, USA
SOURCE: Endocrinology (2000), 141(9), 3072-3079
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The central melanocortin system has been demonstrated to play a pivotal role in energy homeostasis. **Genetic** disruption of this system causes obesity in both humans and mice. Previous expts. have shown that centrally-administered melanocortin agonists inhibit **food intake** and stimulate oxygen consumption. Here we report that centrally-administered melanocortin agonists also inhibit basal insulin release, and alter glucose tolerance. Furthermore, increased plasma insulin levels occur in the young lean **MC4-R** knockout (MC4-RKO) mouse, and impaired insulin tolerance takes place before the onset of detectable hyperphagia or obesity. These data suggest that the central melanocortin system regulates not only energy intake and

expenditure, but also processes related to energy partitioning, as indicated by effects on insulin release and peripheral insulin responsiveness. Previous studies emphasize the role of excess adipose mass in the development of tissue insulin resistance, leading to type II diabetes. The data presented here show that defects in the central control of glucose homeostasis may be an addnl. factor in some types of obesity-assocd. type II diabetes.

REFERENCE COUNT: 38
REFERENCE(S):
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(2) Boden, G; published erratum appears in Diabetes 1997, V46(3), P536 HCAPLUS
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(4) Cheung, C; Endocrinology 1997, V138, P4489 HCAPLUS
(6) Cowley, M; Neuron 1999, V24, P155 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 13 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:584002 HCAPLUS
DOCUMENT NUMBER: 134:51805
TITLE: Role of the **melanocortin-4** receptor in metabolic rate and **food intake** in mice
AUTHOR(S): Chen, Airu S.; Metzger, Joseph M.; Trumbauer, Myrna E.; Guan, Xiao-Ming; Yu, Hong; Frazier, Easter G.; Marsh, Donald J.; Forrest, Michael J.; Gopal-Truter, Shobhna; Fisher, Jill; Camacho, Ramon E.; Strack, Alison M.; Mellin, Theodore N.; MacIntyre, D. Euan; Chen, Howard Y.; Van der Ploeg, Lex H. T.
CORPORATE SOURCE: Merck Research Laboratories, Department of Metabolic Disorders, NJ, USA
SOURCE: Transgenic Res. (2000), 9(2), 145-154
CODEN: TRSEES; ISSN: 0962-8819
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We evaluated the role of the **melanocortin-4** receptor (MC-4R) in the control of metabolic rate and **food intake** in mice. I.p. administration of the non-selective MC-R agonist melanotan II (MT-II; a cyclic heptapeptide) increases metabolic rate in wild-type mice, while MC-4R knockout mice are insensitive to the effects of MT-II on metabolic rate. MC-4R knockout mice are also insensitive to the effects of MT-II on reducing **food intake**. We conclude that MC-4R can mediate control of both metabolic rate and **food intake** in mice. We infer that a role for MC-3R in mediating the acute effects of MT-II on basal metabolic rate and **food intake** in wild-type mice seems limited.

REFERENCE COUNT: 36
REFERENCE(S):
(1) Boston, B; Science 1997, V278, P1641 HCAPLUS
(2) Breslow, M; Am J Physiol 1999, V276, PE443 HCAPLUS
(4) Chen, P; Endocrinology 1999, V140, P2645 HCAPLUS
(5) Dinulescu, D; Proc Natl Acad Sci 1998, V95, P12707 HCAPLUS
(6) Elias, C; Neuron 1998, V21, P1375 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 14 OF 47 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:536337 HCAPLUS
DOCUMENT NUMBER: 134:145075
TITLE: Mahogany (1377-1428) enters brain by a saturable transport system
AUTHOR(S): Kastin, Abba J.; Akerstrom, Victoria
CORPORATE SOURCE: Veterans Affairs Medical Center and Tulane University School of Medicine, New Orleans, LA, USA
SOURCE: J. Pharmacol. Exp. Ther. (2000), 294(2), 633-636
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mouse mahogany **gene** encodes a protein that is involved in the suppression of diet-induced obesity. We studied the ability of its widely conserved C-terminal fragment to cross the blood-brain barrier (BBB) in mice. Multiple-time regression anal. showed that the entry rate (Ki) of 125I-mahogany (1377-1428) from blood-to-brain was 5.5.times.10-4 ml/g.cntdot.min. After coinjection of unlabeled mahogany (1377-1428), the Ki was significantly decreased, showing the self-inhibition characteristic of a saturable transport mechanism. The excess mahogany (1377-1428) did not change the influx rate of 99mTc-albumin, the vascular control, indicating a lack of disruption of the BBB. Statistically significant cross-inhibition was not seen with agouti-related protein (83-132), melanin-concg. hormone, epidermal **growth** factor, leptin, a **melanocortin-4** receptor antagonist, or .alpha.-MSH.
HPLC showed that most of the injected 125I-mahogany (1377-1428) reached the brain intact, and capillary depletion with washout showed that most of it reached the parenchyma. There was no brain-to-blood efflux system for mahogany (1377-1428) but rather retention after i.c.v. administration, and the octanol/buffer partition coeff. showed low lipophilicity. Thus, the results show that the C-terminal peptide product encoded by the mahogany **gene** crosses the BBB by a transport mechanism that is saturable.
The ability of this system to be regulated indicates the therapeutic potential of mahogany (1377-1428) in the treatment of obesity.

REFERENCE COUNT: 22
REFERENCE(S):
(1) Banks, W; Methods in Enzymology 1989, V168, P652 HCAPLUS
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(4) Banks, W; Peptides 1996, V17, P305 HCAPLUS
(6) Dinulescu, D; Proc Natl Acad Sci USA 1998, V95, P12707 HCAPLUS
(7) Egleton, R; Peptides 1997, V18, P1431 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 15 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:491308 HCAPLUS
DOCUMENT NUMBER: 133:206342
TITLE: Melanocortin-4 receptor mutations are a frequent and heterogeneous cause of morbid obesity
AUTHOR(S): Vaisse, Christian; Clement, Karine; Durand, Emmanuelle; Hercberg, Serge; Guy-Grand, Bernard; Froguel, Philippe
CORPORATE SOURCE: Centre National de la Recherche Scientifique, UPRES A 8090, Institute of Biology of Lille, Lille, Fr.

SOURCE: J. Clin. Invest. (2000), 106(2), 253-262
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English

AB By integrating an agonist satiety signal, provided by alpha-MSH (.alpha.-MSH), and an antagonist signal, provided by agouti-related protein (AGRP), the **melanocortin-4** receptor (**MC4-R**) is a key element in the hypothalamic control of **food intake**. Inactivation of the **gene** encoding this G protein-coupled receptor causes obesity in mice. In humans, frameshift mutations in **MC4-R** cause an early-onset dominant form of obesity in two families. In this study we find a high frequency (4%) of rare heterozygous **MC4-R** mutations in a large population of morbidly obese patients. No such mutations were found in controls. By analyzing the phenotypes of the probands carrying these mutations, we demonstrate that these patients display a common, nonsyndromic form of obesity. Interestingly, functional anal. of the mutant receptors indicates that obesity-assocd. defects in **MC4-R** range from loss of function to constitutive activation. Transmission of these mutations in the families of the carriers indicates a variable expressivity that is not related to the functional severity of the mutations. This variable expressivity of **MC4-R**-assocd. obesity is not due to variations in **genes** for .alpha.-MSH or AGRP. Taken together, these results demonstrate that **MC4-R** mutations are a frequent but heterogeneous **genetic** cause of morbid obesity.

REFERENCE COUNT: 37
REFERENCE(S): (4) Clement, K; Nature 1998, V392, P398 HCAPLUS
(5) Cody, J; Hum Genet 1999, V105, P424 HCAPLUS
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(8) Fan, W; Nature 1997, V385, P165 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 16 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:367376 HCAPLUS
DOCUMENT NUMBER: 133:87398
TITLE: Obesity - a **genetic** disease of adipose tissue?
AUTHOR(S): Arner, Peter
CORPORATE SOURCE: Karolinska Institute, Department of Medicine, CME, M61, Huddinge Hospital, Stockholm, S-141 86, Swed.
SOURCE: Br. J. Nutr. (2000), 83(Suppl. 1), S9-S16
CODEN: BJNUAV; ISSN: 0007-1145
PUBLISHER: CABI Publishing
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with .apprx.80 refs. Although the rapid increase in the prevalence of obesity in many countries suggests that environmental factors (mainly overeating and phys. inactivity) play the most important role in the development of overweight, it is very likely that **genetic** factors also contribute. It appears that one major **gene** in combination with one or several minor **genes** constitute the **genetic** components behind excess accumulation of body **fat** in most obese individuals. However, monogenic obesity

has been described in a few families due to changes in leptin, leptin receptor, prohormone convertase, pro-opiomelanocortin or **melanocortin-4** receptor. None of the monogenic variants is of great importance for common human obesity; the latter **genes** are unknown so far. Results from genomic scans suggest that major obesity **genes** are located on chromosomes 2, 10, 11 and 20. Studies of candidate **genes** indicate that the minor obesity **genes** control important functions of adipose tissue, and that structural variance in these **genes** may alter adipose tissue function in a way that promotes obesity. Such **genes** are .beta.2- and .beta.3-adrenoceptors, hormone-sensitive lipase, tumor necrosis factor alpha, uncoupling protein-1, low-d. lipoprotein receptor, and peroxisome proliferator activator receptor gamma-2. Some of these **genes** may promote obesity by **gene-gene** interactions (for example .beta.3-adrenoceptors and uncoupling protein-1) or **gene** -environment interactions (for example .beta.2-adrenoceptors and phys. activity). Some are important for obesity only among women (for example .beta.2- and .beta.3-adrenoceptors, low-d. lipoprotein receptor and tumor necrosis factor alpha). Few "non-adipose" **genes** have so far shown a firm assocn. to common human obesity, which could suggest that the important **genes** for the development of excess body **fat** also control adipose tissue function.

REFERENCE COUNT: 84
REFERENCE(S):
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(6) Buscher, R; Trends in Pharmacological Sciences 1999, V20, P94 HCAPLUS
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(11) Chagnon, Y; Obesity Research 1998, V6, P76 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 17 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:257766 HCAPLUS
DOCUMENT NUMBER: 133:1023
TITLE: The role of the dorsal vagal complex and the vagus nerve in feeding effects of melanocortin-3/4 receptor stimulation
AUTHOR(S): Williams, Diana L.; Kaplan, Joel M.; Grill, Harvey J.
CORPORATE SOURCE: Department of Psychology, University of Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Endocrinology (2000), 141(4), 1332-1337
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fourth intracerebroventricular (4th-icv) administration of the melanocortin-3/4 receptor (MC3/4-R) agonist, MTII, reduces **food intake**; the antagonist, SHU9199, increases feeding. The dorsal motor nucleus of the vagus nerve (DMX) contains the highest d. of **MC4-R** mRNA in the brain. To explore the possibility that the DMX contributes to 4th-icv **MC4-R** effects, we delivered doses of MTII and SHU9119 that are subthreshold for ventricular

response unilaterally through a cannula centered above the DMX. MTII markedly suppressed 2-h (50%), 4-h (50%), and 24-h (33%) intake. Feeding was significantly increased 4 h (50%) and 24 h (20%) after SHU9119 injections. These results suggest that receptors in the DMX, or the dorsal vagal complex more **generally**, underlie effects obtained with 4th-icv administration of these ligands. We investigated possible vagal mediation of 4th-icv MTII effects by giving the agonist to rats with subdiaphragmatic vagotomy. MTII suppressed 2-, 4-, and 24-h liq. diet intake (.apprx.80%) to the same extent in vagotomized and surgical control rats. We conclude that stimulation or antagonism of MC3/4-Rs in the dorsal vagal complex yields effects on **food intake** that do not require an intact vagus nerve.

REFERENCE COUNT: 34
REFERENCE(S):
(3) Bronstein, D; Brain Res 1992, V587, P269 HCAPLUS
(5) Chan, R; J Comp Neurol 1995, V351, P62 HCAPLUS
(6) Fan, W; Nature 1997, V385, P165 HCAPLUS
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(8) Giraudo, S; Brain Res 1998, V809, P302 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 18 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:175835 HCAPLUS
DOCUMENT NUMBER: 132:217147
TITLE: Melanocortin 4 receptor (MC4-R) as target for the identification of compounds used to treat drug addiction
INVENTOR(S): Duman, Ronald
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000014115	A1	20000316	WO 1999-US19790	19990830
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960227	A1	20000327	AU 1999-60227	19990830
PRIORITY APPLN. INFO.:			US 1998-99104	19980903
			WO 1999-US19790	19990830

AB The invention relates to drug screening assays and therapeutic methods for the treatment of addictive behavior disorders, e.g. cocaine and morphine addiction, using the melanocortin 4-receptor (MC4-R) as the target for intervention. The invention also relates to compds. that antagonize the activity or expression of the MC4-R, and the use of such compds. in the treatment of addictive behavior disorders.

REFERENCE COUNT: 4
REFERENCE(S):
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(4) Hruby; US 4649191 A 1987 HCAPLUS

L20 ANSWER 19 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:128252 HCAPLUS
DOCUMENT NUMBER: 132:289486
TITLE: Genome-wide search for **genes** related to the fat-free body mass in the Quebec family study
AUTHOR(S): Chagnon, Yvon C.; Borecki, Ingrid B.; Perusse, Louis; Roy, Sonia; Lacaille, Michel; Chagnon, Monique; Ho-Kim, My Anh; Rice, Treva; Province, Michael A.; Rao, D. C.; Bouchard, Claude
CORPORATE SOURCE: Physical Activity Sciences Laboratory, Division of Kinesiology, Department of Social and Preventive Medicine, Faculty of Medicine, Laval University, Ste-Foy, PQ, G1K 7P4, Can.
SOURCE: Metab., Clin. Exp. (2000), 49(2), 203-207
CODEN: METAAJ; ISSN: 0026-0495
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Fat**-free mass (FFM) consists mostly of skeletal muscle and bone tissues, and identification of the **genes** and mol. mechanisms involved in the control of FFM would have implications for the understanding of sarcopenia and potentially osteoporesis assocd. with aging, as well as the response to starvation, refeeding, anorexia, and any other conditions in which lean body mass is important. A genome-wide search for **genes** related to body leanness has been completed in the Quebec Family Study (QFS). Microsatellite markers (N = 292) from the 22 autosomal chromosomes were typed. The mean spacing of the markers was 11.9 centimorgans (cM) (range, <0.1 to 41). FFM was calcd. from percent body **fat**, derived from underwater weighing, and body wt. and was adjusted by regression for age and sex effects before anal. A max. of 336 sib pairs or 609 pairs of extended relatives were analyzed using single-point Haseman-Elston regression (SIBPAL and RELPAL) and multipoint variance component (SEGPATH) linkage analyses. Significant linkages were obsd. on chromosomes 15q25-q26 for a CA repeat within the insulin-like **growth** factor 1 receptor (IGF1R) **gene** (Lod score = 3.56) and at 18q12 with D18S877 (Lod score = 3.53) and D18S535 (Lod score = 3.58), 2 markers located 10 cM apart. A moderately significant linkage was also obsd. on chromosome 7p15.3 with the marker D7S1808 (Lod score = 2.72). The most obvious candidate **genes** within the regions identified by these linkages include the IGF1R on 15q and neuropeptide Y (NPY) and **growth** hormone-releasing hormone (GHRH) receptor on 7p. On 18q, the melanocortin receptor 4 (**MC4R**) is not likely the candidate **gene** for the obsd. linkage. This study represents the first genome-wide search for **genes** that may be involved in the regulation of the lean component of body mass in humans.
REFERENCE COUNT: 37
REFERENCE(S):
(5) Chagnon, Y; Int J Obes 1999, V23, P278 HCAPLUS
(7) Chagnon, Y; Mol Med 1997, V3, P663 HCAPLUS

(8) Clement, K; Nature 1998, V392, P398 HCAPLUS
(9) Comuzzie, A; Nat Genet 1997, V15, P273 HCAPLUS
(11) Fan, W; Nature 1997, V385, P165 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 20 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:117783 HCAPLUS
DOCUMENT NUMBER: 133:115728
TITLE: A missense variant of the porcine **melanocortin -4** receptor (**MC4R**) **gene** is associated with fatness, **growth**, and **feed** intake traits
AUTHOR(S): Kim, Kwan Suk; Larsen, Niels; Short, Tom; Plastow, Graham; Rothschild, Max F.
CORPORATE SOURCE: Department of Animal Science, Iowa State University, Ames, IA, 50011, USA
SOURCE: Mamm. Genome (2000), 11(2), 131-135
CODEN: MAMGEC; ISSN: 0938-8990
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Our knowledge of the **genetic** factors affecting obesity is increasing, but information about the individual **gene** effects remains limited in humans as well as in animal models. The **melanocortin-4** receptor **gene** (**MC4R**) has been implicated in the regulation of feeding behavior and body wt. in humans and mice. We have studied **MC4R** as a candidate **gene** for the control of economically important **growth** and performance traits in the pig. A missense mutation was identified in a region highly conserved among melanocortin receptor (MCR) **genes** . To det. whether there was an assocn. of this **MC4R** **polymorphism** with phenotypic variation, we tested the mutation in a large no. of individual animals from several different pig lines. Analyses of **growth** and performance test records showed significant assocns. of **MC4R** genotypes with backfat and **growth** rate in a no. of lines as well as **feed** intake overall. It is probable that the variant amino acid residue of the **MC4R** mutation (or a closely linked mutation) causes a significant change of the **MC4R** function. These results support the functional significance of a pig **MC4R** missense mutation and suggest that comparative genomics based on model species may be equally important for application to farm animals as they are for human medicine.
REFERENCE COUNT: 36
REFERENCE(S): (1) Andersson, L; Ann Med 1996, V28, P5 HCAPLUS
(2) Andersson, L; Science 1994, V263, P1771 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 21 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:98833 HCAPLUS
DOCUMENT NUMBER: 132:162049
TITLE: Porcine **melanocortin-4** receptor

gene and use as a **genetic** marker for **fat** content, **weight gain**, and/or **feed** consumption of animals
INVENTOR(S): Rothschild, Max F.; Larson, Niels J.; Kim, Kwan Suk
PATENT ASSIGNEE(S): Iowa State University Research Foundation, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006777	A2	20000210	WO 1999-US16862	19990726
WO 2000006777	A3	20000511		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9952301	A1	20000221	AU 1999-52301	19990726
PRIORITY APPLN. INFO.:			US 1998-94287	19980727
			US 1999-116186	19990115
			WO 1999-US16862	19990726

AB **Genetic** markers in the porcine **melanocortin-4** receptor (**MC4R**) **gene** are disclosed which are assocd. with **fat** content, **growth** rate, and **feed** consumption. Further, novel sequence data from regions of the **gene** are disclosed which may be used in a PCR test to screen for the presence of the marker. The **genetic** marker may be used to screen animals for breeding purposes which have the desired traits regarding **fat** content, **growth** rate, and **feed** consumption. The screening methods disclosed in the invention involve analyzing animals for a **polymorphism** in the **MC4R** **gene**, and test kits which take advantage of the PCR test are also disclosed.

L20 ANSWER 22 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:74150 HCAPLUS
DOCUMENT NUMBER: 132:217324
TITLE: Differential Regulation of Melanin-Concentrating Hormone and Orexin **Genes** in the Agouti-Related Protein/Melanocortin-4 Receptor System
AUTHOR(S): Hanada, Reiko; Nakazato, Masamitsu; Matsukura, Shigeru; Murakami, Noboru; Yoshimatsu, Hironobu; Sakata, Toshiie
CORPORATE SOURCE: Department of Internal Medicine I, School of Medicine, Oita Medical University, Oita, 879-5593, Japan
SOURCE: Biochem. Biophys. Res. Commun. (2000), 268(1), 88-91
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Agouti protein and agouti-related protein (AGRP) antagonize .alpha.-MSH that binds to and activates the **melanocortin-4** receptor (**MC4-R**) in the hypothalamus, thereby stimulating **food intake**. Melanin-concg. hormone (MCH) and orexin are orexigenic peptides that specifically are synthesized in the lateral hypothalamus. MCH **gene** expression was augmented in Ay/a (agouti) mice which overexpress agouti protein, but orexin mRNA was not. AGRP administered intracerebroventricularly into wild-type rats augmented MCH but not orexin **gene** expression. Also, SHU9119, a peptidergic antagonist of **MC4-R**, increased only MCH mRNA. These findings indicate that interruption of signaling at **MC4-R** activates the MCH but not the orexin **gene** . The biosyntheses of MCH and orexin are regulated through different pathways. (c) 2000 Academic Press.
REFERENCE COUNT: 22
REFERENCE(S): (1) Bultman, S; Cell 1992, V71, P1195 HCAPLUS
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(5) Fan, W; Nature 1997, V385, P165 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 23 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:62392 HCAPLUS
DOCUMENT NUMBER: 132:217850
TITLE: Profound obesity associated with a balanced translocation that disrupts the SIM1 **gene**
AUTHOR(S): Holder, J. Lloyd, Jr.; Butte, Nancy F.; Zinn, Andrew R.
CORPORATE SOURCE: Eugene McDermott Center for Human Growth and Development and Department of Internal Medicine, The University of Texas Southwestern Medical School, Dallas, TX, 75235, USA
SOURCE: Hum. Mol. Genet. (2000), 9(1), 101-108
CODEN: HMGEE5; ISSN: 0964-6906
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Studies of mice and humans have revealed a no. of **genes** that when mutated result in severe obesity. The authors have studied a unique girl with early-onset obesity and a de novo balanced translocation between chromosomes 1p22.1 and 6q16.2. Her wt. gain is most likely due to excessive **food intake**, since measured energy expenditure was normal. The authors cloned and sequenced both translocation breakpoints. The translocation does not appear to affect any transcription unit on 1p, but it disrupts the SIM1 **gene** on 6q. SIM1 encodes a human homolog of Drosophila Sim (Single-minded), a transcription factor involved in midline neurogenesis, and is a prototypical member of the bHLH-PAS (basic helix-loop-helix + period, aryl hydrocarbon receptor, Single-minded) **gene** family. Our subject's trans- location separates the 5' promoter region and bHLH domain from the 3' PAS and putative transcriptional regulation domains. The transcriptional targets of SIM1 are not known. Mouse Sim1 is expressed in the developing kidney and central nervous system, and is essential for

formation of the supraoptic and paraventricular (PVN) nuclei of the hypothalamus. Previous neuroanatomical and pharmacol. studies have implicated the PVN in the regulation of body wt.: PVN neurons express the **melanocortin 4** receptor and appear to be physiol. targets of .alpha.-MSH, which inhibits **food intake**. The authors hypothesize that haploinsufficiency of SIM1, possibly acting upstream or downstream of the **melanocortin 4** receptor in the PVN, is responsible for severe obesity in this subject.

REFERENCE COUNT: 52
REFERENCE(S): (1) Chen, H; Cell 1996, V84, P491 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 24 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:805497 HCAPLUS
DOCUMENT NUMBER: 132:121089
TITLE: Functional characterization of mutations in melanocortin-4 receptor associated with human obesity
AUTHOR(S): Ho, Guyu; MacKenzie, Robert G.
CORPORATE SOURCE: Department of Cell Biology, Parke-Davis Pharmaceutical Research, Ann Arbor, MI, 48105, USA
SOURCE: J. Biol. Chem. (1999), 274(50), 35816-35822
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Melanocortin-4** receptor (**MC4R**) is a G protein-coupled receptor implicated in the regulation of body wt. **Genetic** studies in humans have identified two frameshift mutations of **MC4R** assocd. with a dominantly inherited form of obesity. The authors have **generated** and expressed the corresponding **MC4R** mutants in 293T cells and found that cells transfected with the truncation mutants failed to exhibit agonist binding or responsiveness despite retention of structural motifs potentially sufficient for binding and signaling. Immunofluorescence studies showed that the mutant proteins were expressed and localized in the intracellular compartment but absent from the plasma membrane, suggesting that these mutations disrupted the proper cellular transport of **MC4R**. Further studies identified a sequence in the cytoplasmic tail of **MC4R** necessary for the cell surface targeting. The authors further investigated a possible dominant-neg. activity of the mutants on wild-type receptor function. Co-transfection studies showed that the mutants affected neither signaling nor cell surface expression of wild-type **MC4R**. The authors also characterized three human sequence variants of **MC4R**, but these exhibited identical affinities for peptide ligands and identical agonist responsiveness. Thus, unlike the obesity-assocd. **MC4R** truncation mutants, the **polymorphisms** of **MC4R** are unlikely to be contributors to human obesity.

REFERENCE COUNT: 50
REFERENCE(S): (1) Bockaert, J; EMBO J 1999, V18, P1723 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 25 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:764612 HCAPLUS
DOCUMENT NUMBER: 132:220252
TITLE: Agouti antagonism of melanocortin receptors: central and peripheral effects on obesity and diabetes
AUTHOR(S): Mynatt, Randall L.
CORPORATE SOURCE: Pennington Biomedical Research Center, Baton Rouge, LA, 70808, USA
SOURCE: Pennington Cent. Nutr. Ser. (1999), 9(Nutrition, Genetics, and Obesity), 306-319
CODEN: PCNSEW; ISSN: 1063-8822
PUBLISHER: Louisiana State University Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 41 refs. Agouti was the first of several recently cloned **genes** in which mutations lead to obesity in mice. Agouti protein normally functions as a secreted protein acting in a paracrine manner to regulate coat color in mammals. In melanocytes, agouti antagonizes the binding of .alpha.-MSH (.alpha.-MSH) to melanocortin receptor-1 (MC1-R), causing a switch from synthesis of black pigments to yellow pigment. Several dominant mutations at agouti cause the ectopic expression of wild type agouti resulting in a condition similar to adult-onset obesity and non-insulin-dependent diabetes mellitus. Melanocortin receptors are a group of five membrane spanning proteins coupled to G-proteins that activate adenylate cyclase in many tissues. Agouti protein is thought to mimic the natural antagonism of melanocortin receptors to cause obesity. In addn. to its role in melanogenesis, .alpha.-MSH is also a potent inhibitor of **food intake**. Targeted mutagenesis of **MC4-R** recapitulates several of the characteristic features of agouti-induced obesity. The endogenous antagonist of **MC4-R** appears to be an agouti-related protein AGRP which is expressed in the brain and adrenals. Transgenic mice that over express AGRP also become obese. A current model is that agonism, via .alpha.-MSH, of **MC4-R** causes a tonic inhibition of **food intake** that is blocked in the presence of AGRP. Therefore it seems that the primary mechanism of agouti-induced obesity in mice is to mimic the normal antagonism of brain melanocortin receptors. However, the specific area of the brain and/or cell types being influenced by ARGP and melanocortins has not been confirmed.
REFERENCE COUNT: 41
REFERENCE(S): (1) Buffey, J; Pigment Cell Res 1993, V6(6), P385 HCAPLUS
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(3) Chen, W; Cell 1997, V91, P789 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 26 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:764610 HCAPLUS
DOCUMENT NUMBER: 132:102922

TITLE: **Genetics** of obesity: role of neuropeptide Y, norepinephrine, and dopamine
AUTHOR(S): Palmiter, Richard D.; Marsh, Don J.; Hollopeter, Gunther; Szczypka, Mark S.; Thomas, Steve A.
CORPORATE SOURCE: Howard Hughes Medical Institute and Dept. of Biochemistry, University of Washington, Seattle, WA, 98195, USA
SOURCE: Pennington Cent. Nutr. Ser. (1999), 9(Nutrition, Genetics, and Obesity), 269-286
CODEN: PCNSEW; ISSN: 1063-8822
PUBLISHER: Louisiana State University Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 21 refs. Mouse mol. **genetics** has made great strides in identifying **genes** that are involved in the regulation of appetite and metabolic rate-major determinants of body wt. Defects in this regulation are thought to be responsible for some forms of obesity. The products of some of the **genes** involved can be linked into a pathway that relays information about energy stores (**fat**) to regulation of appetite. In particular, a pathway from (a) leptin, that is produced by adipose tissue, to (b) its receptor on pro-opiomelanocortin-producing cells in the hypothalamus that release (c) melanocortins that pos. regulate (d) **melanocortin-4** receptors (**MC4-R**) on post-synaptic cells is taking shape. The cells bearing **MC4-R** are also hypothesized to be neg. regulated by agouti-related protein (AGRP) and neuropeptide Y (NPY). When the cells bearing **MC4-R** are activated they are postulated to inhibit appetite, but the neuromodulators and the post-synaptic cells involved remain to be elucidated. There are undoubtedly many other inputs that regulate appetite and metabolic rate. The authors have examd. the role of specific candidate **gene** products by inactivating the **genes** in mice responsible for their synthesis and assessing the consequences on feeding and metab. The authors have shown that neither NPY nor norepinephrine are essential for normal regulation of appetite or metabolic rate. However, dopamine is absolutely essential for appetite. Without dopamine, mice will not eat or drink. These **genetic** results are inconsistent with a lot of physiol. and pharmacol. data and raise questions about the importance of these modulators as well as the potential for activation of compensatory pathways.

REFERENCE COUNT: 21
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 27 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:673426 HCAPLUS
DOCUMENT NUMBER: 132:11220
TITLE: Monogenic disorders of obesity and body fat distribution
AUTHOR(S): Chen, Dali; Garg, Abhimanyu
CORPORATE SOURCE: Department of Internal Medicine and the Center for Human Nutrition, University of Texas Southwestern

Medical Center, Dallas, TX, 75235-9052, USA
SOURCE: J. Lipid Res. (1999), 40(10), 1735-1746
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 132 refs. Recently, great progress has been made towards understanding the mol. basis of body **fat** regulation. Identification of mutations in several **genes** in spontaneous monogenic animal models of obesity and development of transgenic models have indicated the physiol. roles of many **genes** in the regulation of body **fat** distribution. In humans, mutations in leptin, leptin receptor, prohormone convertase 1 (PC1), pro-opiomelanocortin (POMC), **melanocortin 4**-receptor (**MC4-R**), and peroxisome proliferator-activated receptor (PPAR) .gamma.2 **genes** have been described in patients with severe obesity. Most of these obesity disorders exhibit a distinct phenotype with varying degrees of hypothalamic and pituitary dysfunction and a recessive inheritance, whereas **MC4-R** mutation has a nonsyndromic phenotype with dominant inheritance. These mutations suggest the crit. role of central signaling systems composed of leptin/leptin receptor and .alpha.-MSH/**MC4-R** in human energy homeostasis. Although the **genetic** basis of monogenic disorders of body **fat** distribution, such as congenital **generalized** lipodystrophy and familial partial lipodystrophy, Dunnigan variety, is still unknown, the **genes** for these have recently been localized to chromosomes 9q34 and 1q21-22, resp. The advances in our knowledge of the phenotypic manifestations and underlying mol. mechanisms of **genetic** body **fat** disorders may lead to better treatment and prevention of obesity and other disorders of adipose tissue in the future.

REFERENCE COUNT: 132
REFERENCE(S):
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(4) Banerjee, P; Nat Genet 1998, V18, P177 HCAPLUS
(5) Benjannet, S; Proc Natl Acad Sci 1991, V88, P3564 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 28 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:487144 HCAPLUS
DOCUMENT NUMBER: 131:111438
TITLE: Screening compounds useful in the regulation of body weight using the melanocortin 4 receptor
INVENTOR(S): Lee, Frank; Huszar, Dennis; Gu, Wei
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: U.S., 47 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5932779	A	19990803	US 1997-780749	19970108
US 5908609	A	19990601	US 1996-662560	19960610
CA 2257857	AA	19971218	CA 1997-2257857	19970609
WO 9747316	A1	19971218	WO 1997-US9969	19970609
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9733836	A1	19980107	AU 1997-33836	19970609
AU 723135	B2	20000817		
EP 915706	A1	19990519	EP 1997-929878	19970609
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1227496	A	19990901	CN 1997-197215	19970609
BR 9709684	A	20000509	BR 1997-9684	19970609
PRIORITY APPLN. INFO.:			US 1996-662560	19960610
			US 1997-870511	19970606
			US 1997-780749	19970108
			WO 1997-US9969	19970609

AB The role of the **melanocortin 4**-receptor (**MC4-R**) in the regulation of body wt. is investigated and methods that can be used to screen for compds. affecting function of the receptor and that may be used in the treatment of body wt. disorders, such as obesity, anorexia and cachexia are described. Homozygous **MC4-R** knockout mice showed rapid wt. gain compared to control littermates and were twice as heavy after 15 wk. Heterozygous knockout mice showed an intermediate wt. gain and **generally** showed phenotypes intermediate to wild-type and and homozygous knockout mice. The homozygous knockouts were also significantly longer than control mice and showed increased **food intake**; were hyperinsulinemic and showed raised serum leptin levels. The Agouti **gene** product was shown to be a ligand for **MC4-R** and MC1-R.

REFERENCE COUNT: 60

REFERENCE(S):
(1) Adan; Eur J Pharmacol 1994, V269, P331 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 29 OF 47 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:437196 HCAPLUS
DOCUMENT NUMBER: 131:197653
TITLE: Adipose tissue as an endocrine organ regulating growth, puberty, and other physiological functions
AUTHOR(S): Pankov, Yu. A.
CORPORATE SOURCE: Endocrinology Research Center, Russian Academy of Medical Sciences, Moscow, 115478, Russia
SOURCE: Biochemistry (Moscow) (1999), 64(6), 601-609
CODEN: BIORAK; ISSN: 0006-2979
PUBLISHER: MAIK Nauka/Interperiodica Publishing

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 41 refs. There are reports on some patients with clearly manifested specific features of genotype and phenotype similar to those of ob/ob and db/db mice. Three patients from Turkey were described who had a homozygous mutation in the **gene** of leptin identical to the mutation in C57BL6J ob/ob mice. This mutation is a C .fwdarw. T substitution in codon 105 of the amino acid sequence of leptin. In mice this mutation **generates** a stop-codon; in humans it substitutes Arg-105 with Trp. The mutant human leptin cannot be secreted by the cells and thus has no effect on the hypothalamus. Patients with a homozygous mutation of the leptin receptor resulting in the G .fwdarw. T substitution in the splice donor site of exon 16 were studied in a family of Kabilian origin. Exon 16 was not included in the mature mRNA mol., and a truncated leptin receptor was synthesized which lacked the transmembrane and intracellular domains; this receptor was unable to transduce the hormonal signal. Both groups of patients suffered from obesity, delayed linear **growth**, infertility, increased blood insulin level, and other disorders. Leptin influences lipid metab. by stimulating the expression of the proopiomelanocortin (POMC) **gene** in melanocortinergic neurons of the hypothalamus. POMC is the precursor of .alpha.-MSH (.alpha.-MSH), which binds to the melanocortin receptor **MC4-R** in the brain, decreases appetite, and activates lipid metab. Patients with mutations in **MC4-R** suffered only from obesity, but their **growth** and puberty were not affected. Thus, leptin apparently stimulates **growth** and puberty not through its binding to the receptors on melanocortinergic neurons, but through its binding to receptors on other hypothalamic neurons; this effect of leptin is not affected by mutations in the **MC4-R gene**

REFERENCE COUNT: 41
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 30 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:248879 HCAPLUS
DOCUMENT NUMBER: 131:57387
TITLE: Several mutations in the melanocortin-4 receptor **gene** including a nonsense and a frameshift mutation associated with dominantly inherited obesity in humans
AUTHOR(S): Hinney, A.; Schmidt, A.; Nottebom, K.; Heibult, O.; Becker, I.; Ziegler, A.; Gerber, G.; Sina, M.; Gorg, T.; Mayer, H.; Siegfried, W.; Fichter, M.; Remschmidt, H.; Hebebrand, J.
CORPORATE SOURCE: Clinical Research Group, Department of Child and Adolescent Psychiatry, University of Marburg, Marburg, 35033, Germany
SOURCE: J. Clin. Endocrinol. Metab. (1999), 84(4), 1483-1486
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **melanocortin-4** receptor **gene** (**MC4-R**) has been implicated in wt. regulation. Recently, two independent groups reported frameshift mutations assocd. with a dominant form of obesity. The authors screened the coding region of the **MC4-R** in 306 extremely obese children and adolescents (mean body mass index: BMI 34.4 kg/m2), 25 healthy underweight students (mean BMI 17.1 kg/m2), 52 normal wt. individuals (mean BMI 22.0 kg/m2), 51 in-patients with anorexia nervosa (AN, DSM IV criteria, mean BMI 14.3 kg/m2) and 27 patients with bulimia nervosa (BN, DSM IV criteria, mean BMI 21.7 kg/m2) by single strand conformation **polymorphism** anal. (SSCP). Several mutations were identified, including the frameshift mutation previously described. The mutations were as follows: the deletion of 4 bp (.DELTA. of CTCT at codon 211) results in a frameshift, thus rendering a truncated protein. This mutation has been assumed to be assocd. with dominantly-inherited morbid obesity in humans. Both the index patient (BMI 42.06 kg/m2, height 171 cm, age 19.6 yr) and her mother (BMI 37.55 kg/m2, height 164 cm, age 42.5 yr) were heterozygous for the deletion. A nonsense mutation at position 35 of the **MC4-R** was detected in two obese probands (BMI 31.29 kg/m2 and BMI 45.91 kg/m2). This mutation leads to a truncated protein that encompasses the N-terminal extracellular domain. Both carriers addnl. showed a missense mutation (Asp-37-Val). In both of these cases Tyr-35-Stop and Asp-37-Val were maternally transmitted; thus these variations form a haplotype. A male obese proband harbored two missense mutations (Ser-30-Phe, Gly-252-Ser). Four different missense mutations (Pro-78-Leu, Thr-112-Met, Arg-165-Trp, Ile-317-Thr) were detected in four different male probands. All of these mutations were found solely in extremely obese individuals whose BMIs were all above the 99th percentile. A silent mutation (C-579-T, Val-193-Val) was detected in a male underweight individual. A previously described **polymorphism** (Val-103-Ile) was detected with similar frequencies in all different study groups. The authors identified a novel **polymorphism** (Ile-251-Leu) with similar allele frequencies in all groups under study. In conclusion, the authors' data indicate that mutations in the **MC4-R** are not uncommon. Whereas the authors' data support the evidence for dominantly inherited obesity as revealed by the three obese probands with haploinsufficiency, the functional significance of the missense mutations remains to be detd.
REFERENCE COUNT: 22
REFERENCE(S):
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(2) Clement, K; Nature 1998, V392, P398 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 31 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:246481 HCAPLUS
DOCUMENT NUMBER: 131:86044
TITLE: Melanocortin-4 receptor: a novel signalling pathway involved in body weight regulation
AUTHOR(S): Fisher, S. L.; Yagaloff, K. A.; Burn, P.
CORPORATE SOURCE: Department of Metabolic Diseases, Hoffmann LaRoche,

Nutley, NJ, 07110, USA
SOURCE: Int. J. Obes. (1999), 23(Suppl. 1), 54-58
CODEN: IJOBDP; ISSN: 0307-0565
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 37 refs. For many years, **genetically** obese mouse strains have provided models for human obesity. The Avy/-agouti mouse, one of the oldest obese mouse models, is characterized by maturity-onset obesity and diabetes as a result of ectopic expression of the secreted protein hormone, agouti protein. Agouti protein is normally expressed in hair follicles to regulate pigmentation through antagonism of the melanocortin-1 receptor, but in-vitro studies have demonstrated that the hormone also has potent antagonist activity for the **melanocortin -4** receptor (**MC4-R**). Subsequent development of the **MC4-R** knockout mouse model demonstrated that **MC4-R** plays a role in wt. homeostasis as these mice recapitulated the metabolic defects of the agouti mouse. Further evidence for this hypothesis was obtained from pharmacol. studies utilizing peptides with **MC4-R** agonist activity, that inhibited **food intake** (when administered intracerebrally). Addnl. studies with peptide antagonists have now implicated the **MC4-R** in the leptin signaling pathway. Finally, evidence that the **MC4-R** may play a role in human obesity has been obtained from the identification of a dysfunctional variant of the receptor in **genetically** obese subjects.
REFERENCE COUNT: 37
REFERENCE(S): (1) Adan, R; Peptides 1997, V18, P1279 HCAPLUS
(2) Barsh, G; Trends Gene 1996, V12, P299 HCAPLUS
(3) Boston, B; Science 1997, V278, P1641 HCAPLUS
(5) Bultman, S; Cell 1992, V71, P1195 HCAPLUS
(6) Campfield, L; Endocrin Metab 1997, V4, P81 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 32 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:196123 HCAPLUS
DOCUMENT NUMBER: 131:16920
TITLE: The mahogany protein is a receptor involved in suppression of obesity
AUTHOR(S): Nagle, Deborah L.; McGrail, Sonja H.; Vitale, James; Woolf, Elizabeth A.; Dussault, Barry J., Jr.; DiRocco, Lisa; Holmgren, Lisa; Montagno, Jill; Bork, Peer; Huszar, Dennis; Fairchild-Huntress, Victoria; Ge, Pei; Keilty, John; Ebeling, Chris; Baldini, Linda; Gilchrist, Julie; Burn, Paul; Carlson, George A.; Moore, Karen J.
CORPORATE SOURCE: Millennium Pharmaceuticals, Inc., Cambridge, MA, 02139, USA
SOURCE: Nature (London) (1999), 398(6723), 148-152
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Genetic** studies have shown that mutations within the mahogany locus' suppress the pleiotropic phenotypes, including obesity, of the agouti-lethal-yellow mutant. Here the authors identify the mahogany

gene and its product; this study, to our knowledge, represents the first positional cloning of a suppressor **gene** in the mouse. Expression of the mahogany **gene** is broad; however, in situ hybridization anal. emphasizes the importance of its expression in the ventromedial hypothalamic nucleus, a region that is intimately involved in the regulation of body wt. and feeding. The authors present new **genetic** studies that indicate that the mahogany locus does not suppress the obese phenotype of the **melanocortin-4** -receptor null allele or those of the monogenic obese models (Lepdb, tub and Cpefat). However, mahogany can suppress diet-induced obesity, the mechanism of which is likely to have implications for therapeutic intervention in common human obesity. The amino-acid sequence of the mahogany protein suggests that it is a large, single-transmembrane-domain receptor-like mol., with a short cytoplasmic tail contg. a site that is conserved between Caenorhabditis elegans and mammals. The authors propose two potential, alternative modes of action for mahogany: one draws parallels with the mechanism of action of low-affinity proteoglycan receptors such as fibroblast **growth** factor and transforming **growth** factor-.beta., and the other suggests that mahogany itself is a signaling receptor.

REFERENCE COUNT: 30
REFERENCE(S):
(1) Altschul, S; J Mol Biol 1990, V215, P403 HCAPLUS
(2) Bork, P; J Mol Biol 1994, V236, P1277 HCAPLUS
(3) Bork, P; Mol Biol 1993, V231, P539 HCAPLUS
(5) Dinulescu, D; Proc Natl Acad Sci USA 1998, V95, P12707 HCAPLUS
(7) Duke-Cohan, J; Proc Natl Acad Sci USA 1998, V95, P11336 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 33 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:176704 HCAPLUS
DOCUMENT NUMBER: 130:333088
TITLE: Role of the CNS melanocortin system in the response to overfeeding
AUTHOR(S): Hagan, Mary M.; Rushing, Paul A.; Schwartz, Michael W.; Yagaloff, Keith A.; Burn, Paul; Woods, Stephen C.; Seeley, Randy J.
CORPORATE SOURCE: Department of Psychiatry, University of Cincinnati Medical Center, Cincinnati, OH, 45267-0559, USA
SOURCE: J. Neurosci. (1999), 19(6), 2362-2367
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The voluntary suppression of **food intake** that accompanies involuntary overfeeding is an effective regulatory response to pos. energy balance. Because the pro-opiomelanocortin (POMC)-derived melanocortin system in the hypothalamus promotes anorexia and wt. loss and is an important mediator of energy regulation, the authors hypothesized that it may contribute to the hypophagic response to overfeeding. Two groups of rats were overfed to 105 and 116% of control body wt. via a gastric catheter. In the first group, in situ hybridization was used to measure POMC **gene** expression in the rostral arcuate (ARC). Overfeeding increased POMC mRNA in the ARC by 180% relative to levels in control rats. For rats in the second group, the overfeeding was stopped,

and they were infused intracerebroventricularly with SHU9119 (SHU), a melanocortin (MC) antagonist at the MC3 and **MC4 receptor**, or vehicle. Although SHU (0.1 nmol) had no effect on **food intake** of control rats, intake of overfed rats increased by 265% relative to CSF-treated controls. This complete reversal of regulatory hypophagia not only maintained but actually increased the already elevated wt. of overfed rats, whereas CSF-treated overfed rats lost wt. These results indicate that CNS MCs mediate hypophagic signaling in response to involuntary overfeeding and support the hypothesis that MCs are important in the central control of energy homeostasis.

REFERENCE COUNT: 35
REFERENCE(S):
(1) Adan, R; Mol Pharmacol 1994, V46, P1182 HCAPLUS
(2) Akiyama, T; Diabetes Res Clin Pract 1996, V31, P27 HCAPLUS
(3) Bernstein, I; Proc Soc Exp Biol Med 1975, V150, P546 HCAPLUS
(4) Bronstein, D; Brain Res 1992, V587, P269 HCAPLUS
(5) Cha, M; J Lipid Res 1998, V39, P1655 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 34 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:171285 HCAPLUS
DOCUMENT NUMBER: 130:306689
TITLE: Melanocortin and leptin signaling systems: central regulation of catabolic energy balance
AUTHOR(S): Fisher, Stewart L.; Yagaloff, Keith A.; Burn, Paul
CORPORATE SOURCE: Department of Metabolic Diseases, Hoffmann LaRoche, Inc., Nutley, NJ, 07110, USA
SOURCE: J. Recept. Signal Transduction Res. (1999), 19(1-4), 203-216
CODEN: JRETET; ISSN: 1079-9893
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 34 refs. The recent cloning of the ob **gene** (leptin) has revolutionized the authors' understanding of obesity and the underlying factors that govern wt. homeostasis. There is growing evidence that long term **food intake** regulation is controlled by the central nervous system by a no. of peptide hormones in response to changes in leptin levels. Studies of these hormones, using both **genetic** and pharmacol. approaches, have provided a foundation for decoding the mol. logic of the neuronal circuits which regulate **food intake** control and energy balance. A review of the current progress in the **melanocortin-4** receptor pathway, with particular emphasis on its relation to leptin, neuropeptide Y and other obesity hormones known to modulate wt. homeostasis, is presented.

REFERENCE COUNT: 34
REFERENCE(S):
(1) Barsh, G; Trends in Genetics 1996, V12, P299 HCAPLUS
(2) Boston, B; Science 1997, V278, P1641 HCAPLUS
(3) Bultman, S; Cell 1992, V71, P1195 HCAPLUS
(4) Campfield, L; Endocrin Metab 1997, V4, P81 HCAPLUS
(5) Campfield, L; Horm Metab Res 1996, V28, P619 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 35 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:158557 HCAPLUS
DOCUMENT NUMBER: 130:310193
TITLE: Identification and functional analysis of novel human melanocortin-4 receptor variants
AUTHOR(S): Gu, Wei; Tu, Zhiming; Kleyn, Patrick W.; Kissebah, Ahmed; Duprat, Laura; Lee, John; Chin, Wendy; Maruti, Sanchit; Deng, Nanhua; Fisher, Stewart L.; Franco, Lucia S.; Burn, Paul; Yagaloff, Keith A.; Nathan, Julie; Heymsfield, Steven; Albu, Jeanine; Pi-Sunyer, F. Xavier; Allison, David B.
CORPORATE SOURCE: Millennium Pharmaceuticals, Cambridge, MA, 02139, USA
SOURCE: Diabetes (1999), 48(3), 635-639
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Inactivation of the **melanocortin-4** receptor (**MC4-R**) by **gene**-targeting results in mice that develop maturity-onset obesity, hyperinsulinemia, and hyperglycemia. These phenotypes resemble common forms of human obesity, which are late-onset and frequently accompanied by NIDDM. It is not clear whether sequence variation of the **MC4-R gene** contributes to obesity in humans. Therefore, we examd. the human **MC4-R gene polymorphism** in 190 individuals ascertained on obesity status. Three allelic variants were identified, including two novel ones, Thr112Met and Ile137Thr. To analyze possible functional alterations, the variants were cloned and expressed in vitro and compared with the wild-type receptor. One of the novel variants, Ile137Thr, identified in an extremely obese proband (BMI 57), was found to be severely impaired in ligand binding and signaling, raising the possibility that it may contribute to development of obesity. Furthermore, our results also suggest that sequence **polymorphism** in the **MC4-R** coding region is unlikely to be a common cause of obesity in the population studied, given the low frequency of functionally significant mutations.
REFERENCE COUNT: 17
REFERENCE(S): (1) Bultman, S; Cell 1992, V71, P1195 HCAPLUS
(2) Clement, K; Nature 1998, V392, P398 HCAPLUS
(3) Comuzzie, A; Science 1998, V280, P1374 HCAPLUS
(4) Duhl, D; Nat Genet 1994, V8, P59 HCAPLUS
(5) Fan, W; Nature 1997, V385, P165 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 36 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:150322 HCAPLUS
DOCUMENT NUMBER: 131:40384
TITLE: Absence of **genetic** variation in some obesity candidate **genes** (GLP1R, ASIP, MC4R, MC5R) among Pima Indians
AUTHOR(S): Norman, R. A.; Permana, P.; Tanizawa, Y.; Ravussin, E.
CORPORATE SOURCE: Clinical Diabetes and Nutrition Section, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Phoenix, AZ, USA

SOURCE: Int. J. Obes. (1999), 23(2), 163-165
CODEN: IJOBDP; ISSN: 0307-0565
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective of this study was to examine the obesity candidate **genes** glucagon-like-peptide receptor (GLP1R), agouti signaling protein (ASIP) and the melanocortin receptors 4 and 5 (**MC4R** and MC5R) for **DNA polymorphisms** in their coding regions. Unrelated, non-diabetic Pima Indians (8 to 12 from each extreme of body **fat**) were used in the study. **DNA** sequencing within the coding regions of each **gene** was conducted. Only one variant was detected, a silent substitution in exon 6 of GLP1R. The exclusion of any common amino-acid **polymorphisms** (allele frequency .gtoreq. 0.20). implies that structural variants of these **genes** do not contribute to variation in the high level of obesity obsd. among the Pima Indians.

REFERENCE COUNT: 17
REFERENCE(S): (2) Chagnon, Y; Mol Med 1997, V3, P663 HCAPLUS
(3) Chagnon, Y; Obes Res 1998, V6, P76 HCAPLUS
(4) Chen, W; Cell 1997, V91, P789 HCAPLUS
(5) Gotoda, T; Diabetologia 1997, V40, P976 HCAPLUS
(6) Huszar, D; Cell 1997, V88, P131 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 37 OF 47 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:24311 HCAPLUS
DOCUMENT NUMBER: 130:192117

TITLE: Mice lacking melanin-concentrating hormone are hypophagic and lean

AUTHOR(S): Shimada, Masako; Tritos, Nicholas A.; Lowell, Bradford B.; Flier, Jeffrey S.; Maratos-Flier, Eleftheria
CORPORATE SOURCE: Division of Endocrinology, Beth Israel Deaconess Medical Center, Boston, MA, 02115, USA

SOURCE: Nature (London) (1998), 396(6712), 670-674
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Feeding is influenced by hypothalamic neuropeptides that promote (orexigenic peptides) or inhibit feeding. Of these, neuropeptide Y (NPY) in the arcuate nucleus and melanin-concg. hormone (MCH) and orexins/hypocretins in the lateral hypothalamus have received attention because their expression is increased during fasting and because they promote feeding when administered centrally. Surprisingly, absence of the orexigenic neuropeptide NPY fails to alter feeding or body wt. in normal mice. As deficiency of a single component of the pathway that limits **food intake** (such as leptin or receptors for **melanocortin-4**) causes obesity, it has been suggested that orexigenic signals are more redundant than those limiting **food intake**. To define further the physiol. role of MCH and to test the redundancy of orexigenic signals, we **generated** mice carrying a targeted deletion of the MCH **gene**. MCH-deficient mice have reduced body wt. and leanness due to hypophagia (reduced feeding) and an inappropriately increased metabolic rate, despite their reduced amts. of both leptin and arcuate nucleus

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pro-opiomelanocortin mRNA. Our results show that MCH is a crit. regulator of feeding and energy balance which acts downstream of leptin and the melanocortin system, and that deletion of a **gene** encoding a single orexigenic peptide can result in leanness.

REFERENCE COUNT: 29
REFERENCE(S):
(1) Ahima, R; J Clin Invest 1998, V101, P1020 HCAPLUS
(2) Ahima, R; Nature 1996, V382, P250 HCAPLUS
(4) Bittencourt, J; J Comp Neurol 1992, V319, P218 HCAPLUS
(5) Breton, C; Mol Cell Neurosci 1993, V4, P271 HCAPLUS
(6) de Lecea, L; Proc Natl Acad Sci USA 1998, V95, P322 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 38 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:680014 HCAPLUS
DOCUMENT NUMBER: 130:36269
TITLE: Mahogany (mg) stimulates feeding and increases basal metabolic rate independent of its suppression of agouti
AUTHOR(S): Dinulescu, Daniela M.; Fan, Wei; Boston, Bruce A.; McCall, Kathleen; Lamoreux, M. Lynn; Moore, Karen J.; Montagno, Jill; Cone, Roger D.
CORPORATE SOURCE: Vollum Institute, Departments of Cell and Developmental Biology, Oregon Health Sciences University, Portland, OR, 97201, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1998), 95(21), 12707-12712
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mahogany (mg) locus originally was identified as a recessive suppressor of agouti, a locus encoding a skin peptide that modifies coat color by antagonizing the MSH receptor or MC1-R. Certain dominant alleles of agouti cause an obesity syndrome when ectopic expression of the peptide aberrantly antagonizes the **MC4-R**, a related MSH receptor expressed in hypothalamic circuitry and involved in the regulation of feeding behavior and metab. Recent work has demonstrated that mg, when homozygous, blocks not only the ability of agouti to induce a yellow coat color when expressed in the skin of the lethal yellow mouse (AY), but also the obesity resulting from ectopic expression of agouti in the brain. Detailed anal. of mg/mg AY/a animals, presented here, demonstrates that mg/mg blocks the obesity, hyperinsulinemia, and increased linear **growth** induced by ectopic expression of the agouti peptide. Remarkably, however, mg/mg did not reduce hyperphagia in the AY/a mouse. Furthermore, mg/mg induced hyperphagia and an increase in basal metabolic rate in the C57BL/6J mouse in the absence of AY. Consequently, although mahogany is broadly required for agouti peptide action, it also appears to be involved in the control of metabolic rate and feeding behavior independent of its suppression of agouti.

REFERENCE COUNT: 18
REFERENCE(S):
(1) Bultman, S; Cell 1992, V71, P1195 HCAPLUS
(3) Erickson, J; Science 1996, V274, P1704 HCAPLUS
(4) Fan, W; Nature (London) 1997, V385, P165 HCAPLUS

(6) Gantz, I; J Biol Chem 1993, V268, P15174 HCAPLUS
(7) Graham, M; Nat Genet 1997, V17, P273 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 39 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:677362 HCAPLUS
DOCUMENT NUMBER: 130:47673
TITLE: Feeding effects of hypothalamic injection of melanocortin 4 receptor ligands
AUTHOR(S): Giraudo, Silvia Q.; Billington, Charles J.; Levine, Allen S.
CORPORATE SOURCE: Department of Medicine, University of Minnesota, Minneapolis, MN, USA
SOURCE: Brain Res. (1998), 809(2), 302-306
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has been reported that intraventricular administration of the **melanocortin 4** receptor (**MC4-R**) agonist MT II and antagonist SHU9119 alter **food intake** . We found that MT II and SHU9119 have extremely potent effects on feeding when injected in the paraventricular nucleus (PVN), a site where **MC4-R gene** expression is very high. Our finding provides direct evidence that **MC4-R** signaling is important is mediating **food intake** and that melanocortin neurons in the PVN exert a tonic inhibition of feeding behavior. Chronic disruption of this inhibitory signal is a possible explanation of the agouti-obesity syndrome.
REFERENCE COUNT: 14
REFERENCE(S): (1) Bray, G; Physiol Rev 1979, V59, P719 HCAPLUS
(2) Cone, R; Recent Prog Horm Res 1996, V51, P287 HCAPLUS
(3) Cone, R; Recent Prog Horm Res discussion 1996, P318 HCAPLUS
(4) Fan, W; Nature 1997, V385, P165 HCAPLUS
(5) Huszar, D; Cell 1997, V88, P131 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 40 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:661055 HCAPLUS
DOCUMENT NUMBER: 130:33437
TITLE: Response of neuropeptide Y-deficient mice to feeding effectors
AUTHOR(S): Hollopeter, Gunther; Erickson, Jay C.; Seeley, Randy J.; Marsh, Donald J.; Palmiter, Richard D.
CORPORATE SOURCE: Howard Hughes Medical Institute and Department of Biochemistry, University of Washington, Seattle, WA, 98195, USA
SOURCE: Regul. Pept. (1998), 75-76, 383-389
CODEN: REPPDY; ISSN: 0167-0115
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neuropeptide Y (NPY) is thought to be an important central regulator of feeding behavior and body wt. However, mice lacking NPY due to targeted

genetic deletion do not display abnormalities in **food intake** or body wt. with ad libitum access to food or in response to fasting. In this study, we investigate the response of NPY-deficient (NPY-/-) mice to anorexic and orexigenic treatments. The dose-dependent stimulation of **food intake** by central NPY administration was unaltered in NPY-/- mice. Peripheral administration of various doses of leptin for 2 days elicited a two-fold greater inhibition of **food intake** in NPY-/- mice than in wild-type (NPY+/+) mice. In addn., lateral ventricular administration of leptin (1 .mu.g) suppressed refeeding in NPY-/- mice after a 24 h fast, but had little effect in NPY+/+ mice. However, the response to other feeding inhibitors such as ACTH-releasing factor (CRF), dexfenfluramine, and a **melanocortin 4** receptor (**MC4R**) agonist, MTII, was unaltered in NPY-/- mice. These results indicate that the appetite-suppressant action of exogenous leptin is uniquely amplified in NPY-/- mice, and suggest that NPY may tonically antagonize leptin action.

REFERENCE COUNT: 49

REFERENCE(S):
(1) Ahima, R; Nature 1996, V382, P250 HCAPLUS
(2) Baraban, S; J Neurosci 1997, V17, P8927 HCAPLUS
(3) Baskin, D; Diabetes 1998, V47, P538 HCAPLUS
(4) Beck, B; Int J Obes Relat Metab Disord 1992, V16, P295 HCAPLUS
(5) Billington, C; Am J Physiol 1991, V260, PR321 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 41 OF 47 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:645524 HCAPLUS

DOCUMENT NUMBER: 129:326317

TITLE: A C-terminal fragment of Agouti-related protein increases feeding and antagonizes the effect of alpha-melanocyte stimulating hormone in vivo

AUTHOR(S): Rossi, M.; Kim, M. S.; Morgan, D. G. A.; Small, C. J.; Edwards, C. M. B.; Sunter, D.; Abusnana, S.; Goldstone, A. P.; Russell, S. H.; Stanley, S. A.; Smith, D. M.; Yagaloff, K.; Ghatei, M. A.; Bloom, S. R.

CORPORATE SOURCE: Endocrine Unit, Imperial College School of Medicine, Hammersmith Hospital, London, W12 ONN, UK

SOURCE: Endocrinology (1998), 139(10), 4428-4431
CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Agouti-related protein (Agrp) is present in rat and human hypothalamus and is structurally related to agouti protein. Over-expression of either of these proteins results in obesity. However the effect of exogenous Agrp and its in vivo interaction with .alpha.-MSH, the likely endogenous melanocortin 3 and 4 receptor (MC3-R and **MC4-R**) agonist, have not been demonstrated. We report that 1 nmol of Agrp(83-132), a C-terminal fragment of Agrp, when administered intracerebroventricularly (ICV) into rats, increased **food intake** over a 24-h period (23.0 g saline vs. 32.9 g Agrp). The hyperphagia was similar to that seen when 1 nmol of the synthetic MC3-R and **MC4-R** antagonist SHU 9119 was given ICV (19.6 g saline vs. 32.5 g SHU 9119). Both Agrp(83-132) and SHU 9119 blocked the

redn. in 1-h **food intake** of ICV .alpha.-MSH at the beginning of the dark phase. This effect occurred independently of whether the antagonists were administered simultaneously, or nine hours prior, to the .alpha.-MSH. We have also shown Agrp(83-132) is an antagonist at the MC3-R and **MC4-R**, with similar inhibition of cAMP activation to that previously reported for the full length peptide. In conclusion, Agrp(83-132) administered ICV increases feeding with long lasting effects and is able to inhibit the action of .alpha.-MSH. This interaction may be mediated by the MC3-R and/or **MC4-R**.

L20 ANSWER 42 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:564854 HCAPLUS
DOCUMENT NUMBER: 129:274097
TITLE: Severe early-onset obesity, adrenal insufficiency and red hair pigmentation caused by POMC mutations in humans
AUTHOR(S): Krude, Heiko; Biebermann, heike; Luck, Werner; Horn, Rudiger; Brabant, Georg; Gruters, Annette
CORPORATE SOURCE: Dep. Pediatrics, Humboldt-Univ., Berlin, Germany
SOURCE: Nat. Genet. (1998), 19(2), 155-157
CODEN: NGENEC; ISSN: 1061-4036
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sequential cleavage of the precursor protein pre-pro-opiomelanocortin (POMC) **generates** the melanocortin peptides ACTH (ACTH), melanocyte-stimulating hormones (MSH) .alpha., .beta. and .gamma. as well as the opioid-receptor ligand .beta.-endorphin. While a few cases of isolated ACTH deficiency have been reported (OMIM 201400), an inherited POMC defect has not been described so far. Recent studies in animal models elucidated a central role of .alpha.-MSH in the regulation of **food intake** by activation of the brain **melanocortin-4**-receptor (**MC4-R**; refs 3-5) and the linkage of human obesity to chromosome 2 in close proximity to the POMC locus, led to the proposal of an assocn. of POMC with human obesity. The dual role of .alpha.-MSH in regulating **food intake** and influencing hair pigmentation predicts that the phenotype assocd. with a defect in POMC function would include obesity, alteration in pigmentation and ACTH deficiency. The observation of these symptoms in two probands promoted us to search for mutations within their POMC **genes**. Patient 1 was found to be a compd. heterozygote for two mutations in exon 3 (G7013T, C7133.DELTA.) which interfere with appropriate synthesis of ACTH and .alpha.-MSH. Patient 2 was homozygous for a mutation in exon 2 (C3804A) which abolishes POMC translation. These findings represent the first examples of a **genetic** defect within the POMC **gene** and define a new monogenic endocrine disorder resulting in early-onset obesity, adrenal insufficiency and red hair pigmentation.

L20 ANSWER 43 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:193652 HCAPLUS
DOCUMENT NUMBER: 128:281195
TITLE: Obesity **genes**
AUTHOR(S): Swierczynski, Julian; Kochan, Zdzislaw; Karbowska, Joanna

CORPORATE SOURCE: Katedra i Zaklad Biochem. A. M. Debinki, Gdansk, 80-211, Pol.
SOURCE: Postepy Biochem. (1997), 43(3), 174-182
CODEN: PSTBAH; ISSN: 0032-5422
PUBLISHER: Polskie Towarzystwo Biochemiczne
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Polish

AB A review, with 66 refs. Topics discussed include: obesity **genes** (ob, db, **fat**, tub, agouti); leptin as an important element in the signaling between adipose tissue and the central nervous system (CNS); role of leptin, Ob-R, NPY, MMH, and **MC4-R** in the regulation of **food intake**; leptin as an anti-obesity drug; and adipose tissue as an endocrine organ.

L20 ANSWER 44 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:13857 HCAPLUS
DOCUMENT NUMBER: 128:110853
TITLE: Melanocortin-4 receptor in screening for compounds useful in the regulation of body weight
INVENTOR(S): Lee, Frank; Huszar, Dennis; Gu, Wei
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9747316	A1	19971218	WO 1997-US9969	19970609
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5908609	A	19990601	US 1996-662560	19960610
US 5932779	A	19990803	US 1997-780749	19970108
AU 9733836	A1	19980107	AU 1997-33836	19970609
AU 723135	B2	20000817		
EP 915706	A1	19990519	EP 1997-929878	19970609
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9709684	A	20000509	BR 1997-9684	19970609
PRIORITY APPLN. INFO.:			US 1996-662560	19960610
			US 1997-780749	19970108
			US 1997-870511	19970606
			WO 1997-US9969	19970609

AB The present invention relates to drug-screening assays, and diagnostic and therapeutic methods for the treatment of body wt. disorders, such as obesity, anorexia and cachexia, utilizing the melanocortin 4 receptor (MC4-R) as the target for intervention. - The invention also relates to compds. that modulate the activity or expression of the MC4-R, and the use of such compds. in the treatment of body wt. disorders.

L20 ANSWER 45 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:811280 HCAPLUS
DOCUMENT NUMBER: 128:87433
TITLE: Linkage and association studies between the melanocortin receptors 4 and 5 **genes** and obesity-related phenotypes in the Quebec family study
AUTHOR(S): Chagnon, Yvon C.; Chen, Wen-Ji; Perusse, Louis; Chagnon, Monique; Nadeau, Andre; Wilkison, William O.; Bouchard, Claude
CORPORATE SOURCE: Physical Activity Sciences Laboratory, Laval University, Ste-Foy, PQ, Can.
SOURCE: Mol. Med. (N. Y.) (1997), 3(10), 663-673
CODEN: MOMEF3; ISSN: 1076-1551
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The agouti yellow mouse shows adult onset of moderate obesity and diabetes. A depressed basal lipolytic rate in adipocytes or a decreased adrenergic tone arising from antagonizing .alpha.-MSH (MSH) activation of melanocortin receptors (MCR) could be at the origin of the obesity phenotype. MCR 4 and 5 (**MC4R**, MC5R) **genes** were studied in the Quebec Family Study. Sequence variations were detected by Southern blot probing of restricted genomic **DNA**, and mRNA tissue expression was detected by RT-PCR. Subjects with a wide range of wt. were used for single-point sib-pair linkage studies (max. of 289 sibships from 124 nuclear families). Anal. of variance across genotypes in unrelated males (n=143) and females (n=156) was also undertaken. Body mass index (BMI), sum of six skin-folds (SF6), **fat** mass (FM), percent body **fat** (%**FAT**), RQ (RQ), resting metabolic rate (RMR), fasting glucose and insulin, and glucose and insulin area during an oral glucose tolerance test were analyzed. **MC4R** showed **polymorphism** with NcoI, and MC5R, with PstI and PvuII, with a heterozygosity of 0.38, 0.10, and 0.20, resp. Linages were obsd. between MC5R and BMI (p=0.001), SF6 (p=0.005), FM (p=0.001), and RMR (p=0.002), whereas assocns. were obsd. in females between MC5R and BMI (p=0.003), and between **MC4R** and FM (p=0.002) and %**FAT** (p=0.004). After correction for multiple tests, these p values are lowered by one tenth. **MC4R** and MC5R mRNAs have been detected in brain, adipose tissue, and skeletal muscle. **MC4R** and MC5R exhibit evidence of linkage or assocns. with obesity phenotypes, but this evidence is strongest for MC5R.

L20 ANSWER 46 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:338855 HCAPLUS
DOCUMENT NUMBER: 125:26578
TITLE: Distribution of cDNA of melanocortin receptor subtypes in human tissues
AUTHOR(S): Chhajlani, Vijay
CORPORATE SOURCE: Department Pharmaceutical Pharmacology, Division Pharmaceutical Bioscience, Uppsala, 751 24, Swed.
SOURCE: Biochem. Mol. Biol. Int. (1996), 38(1), 73-80
CODEN: BMBIES; ISSN: 1039-9712
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Distribution of cDNA for five individual melanocortin receptor subtypes in

20 different human tissues was detd. by PCR using subtype specific primers. PCR products were first visualized by agarose gel electrophoresis and ethidium bromide staining, and specific products were identified for melanocortin 1 receptor (MC1R) in pituitary and testis, for MC2R in adrenal gland, for MC3R in heart, for MC5R in adrenal gland, **fat** cells, kidney, leukocytes, lung, lymph node, mammary gland, ovary, pituitary, testis and uterus. The **MC4R** cDNA could not be detected by ethidium bromide staining. More tissues were revealed as pos. when the **DNA** from PCR were hybridized with subtype specific radioactive probes. All the subtypes except **MC4R** could be detected in testis. **MC4R** could only be detected in pituitary. This is the first report describing the comprehensive distribution anal. of melanocortin receptor subtype cDNAs in human tissues, and provides a link between individual receptor subtype and diverse biol. activities of melanocortic peptides in the resp. target tissues.

L20 ANSWER 47 OF 47 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:303597 HCAPLUS
DOCUMENT NUMBER: 122:98525
TITLE: Integration of 28 STSs into the physical map of human chromosome 18
AUTHOR(S): Gerken, Steve; Fish, Kimberlee; Uyar, Denise; Polymeropoulos, Mihael H.; Bradley, Paige; White, Ray; Overhauser, Joan; Silverman, Gary A.
CORPORATE SOURCE: Dep. Hum. Genet., Univ. Utah, Salt Lake City, UT, 84112, USA
SOURCE: Genomics (1994), 24(3), 612-13
CODEN: GNMCEP; ISSN: 0888-7543
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Genes** on human chromosome 18 are assocd. with familial glucocorticoid deficiency, pemphigus vulgaris and foliaceous, familial amyloidosis, colorectal carcinoma, erythropoietic protoporphyria, folicular lymphoma, and congenital methemoglobinemia. As the resoln. of human **genetic** maps improves, linkage between other diseases and specific regions of chromosome 18 will occur. A phys. map of human chromosome 18 will prove useful in identifying candidate **genes** that are assocd. with these disorders. Thus, the purpose of this study was to integrate 9 new transcriptional tags and the **melanocortin 4** receptor and 19 simple sequence repeats into the phys. map of human chromosome 18. The simple sequence repeats were isolated by screening genomic **DNA** libraries constructed in M13mp18 vectors with oligonucleotide probes that detected dinucleotide d(CA)- and tetra-nucleotide-repeat motifs. **Dna** sequences of clones that contained micro-satellite repeats were obtained by thermocycle sequencing, and STSs were developed from clones that contained numerous repeats. STSs that identified highly **polymorphic** loci in eight unrelated CEPH parents were used for genotyping. Results of linkage anal. and ests. of heterozygosity for thes markers will be reported.

=> d stat que

L1 8 SEA FILE=REGISTRY MSHFNLYLILIMCNSIIDPLIYAL/SQSP
L2 941245 SEA FILE=REGISTRY SQL< 50
L4 20 SEA FILE=REGISTRY CAGGGGATAGCAACAGATGA|TTAAGTGGAGGAAGAAGG|CATTA

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                TGACAGTTAAGCGG|CATTATGACAGTTAAGCGG|ATAGCAACAGATGATCTCTTTG/SQSN
L5              4 SEA FILE=REGISTRY L4 AND L2
L6              3 SEA FILE=REGISTRY ("MELANOCORTIN-4 RECEPTOR (112-METHIONINE)
                  (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (137-THREONINE)
                  (HUMAN)"/CN OR "MELANOCORTIN-4 RECEPTOR (HUMAN)"/CN)
L10             1 SEA FILE=HCAPLUS L5
L11           254 SEA FILE=HCAPLUS L6 OR MC4R OR MELANOCORTIN(W)4 OR MC4(W)(R OR
                  RECEPTOR?)
L17           105 SEA FILE=HCAPLUS L11 AND (POLYMORPH? OR FAT OR FEED OR GROWTH
                  OR FOOD(W)(INTAKE OR CONSUMPTION) OR WEIGHT(W)GAIN?)
L18            10 SEA FILE=HCAPLUS L17 AND (PIG? OR PORCINE OR SWINE OR HOG?)
L19            94 SEA FILE=HCAPLUS L11 (L) (POLYMORPH? OR FAT OR FEED OR GROWTH
                  OR FOOD(W)(INTAKE OR CONSUMPTION) OR WEIGHT(W)GAIN?)
L20            47 SEA FILE=HCAPLUS (GENE? OR DNA OR NUCLEIC) AND L19
L21             9 SEA FILE=HCAPLUS L1
L22             6 SEA FILE=HCAPLUS L21 NOT (L10 OR L18 OR L20)

=> d ibib abs hitrn l22 1-6


L22  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2000:547409  HCAPLUS
DOCUMENT NUMBER:          133:145447
TITLE:                    Methods and reagents for discovering and using
                          mammalian melanocortin receptor agonists and
                          antagonists to modulate feeding behavior in animals
INVENTOR(S):              Cone, Roger D.; Fan, Wei; Boston, Bruce A.; Kesterton,
                          Robert A.; Lu, Dongsi; Chen, Wenbiao
PATENT ASSIGNEE(S):       Oregon Health Sciences University, USA
SOURCE:                   U.S., 82 pp., Cont.-in-part of U.S. 5,849,871.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   5
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ----------------  ----  --------       ---------------  --------
     US 6100048         A    20000808       US 1996-706281   19960904
     US 5280112         A    19940118       US 1992-866560   19920410
     US 5837521         A    19981117       US 1993-44812    19930408
     US 5849871         A    19981215       US 1995-466906   19950606
     US 5773229         A    19980630       US 1995-478992   19950607
     WO 9810068         A2   19980312       WO 1997-US15565  19970904
     WO 9810068         A3   19980625
         W:  AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,
             ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,
             LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
             SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG,
             KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
     AU 9741812         A1   19980326       AU 1997-41812    19970904
     AU 719954          B2   20000518
```

EP 935655 A1 19990818 EP 1997-939799 19970904
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
US 6046011 A 20000404 US 1998-105298 19980626
PRIORITY APPLN. INFO.: US 1992-866560 19920410
US 1992-886979 19920521
US 1993-44812 19930408
US 1995-466906 19950606
US 1995-478992 19950607
US 1992-866979 19920410
US 1993-77673 19930615
US 1996-706281 19960904
WO 1997-US15565 19970904

AB The present invention provides recombinant expression constructs comprising nucleic acid encoding mammalian melanocortin receptors, and mammalian cells into which said recombinant expression constructs have been introduced that express functional mammalian melanocortin receptors. The invention provides a panel of such transformed mammalian cells expressing melanocortin receptors for screening compds. for receptor agonist and antagonist activity. The invention also provides methods for using such panels of melanocortin receptor-expressing mammalian cells to specifically detect and identify agonists and antagonists for each melanocortin receptor, as well as patterns of agonist and antagonist activity of said compds. for the class of melanocortin receptors. Such screening methods provide a means for identifying compds. with patterns of melanocortin agonist and antagonist activity which are assocd. with the capacity to influence or modify metab. and behavior, particularly feeding behavior.

IT **201099-18-5**, Melanocortin-4 receptor (human)
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; methods and reagents for discovering and using mammalian melanocortin receptor agonists and antagonists to modulate feeding behavior in animals)

REFERENCE COUNT: 77
REFERENCE(S):
(1) Ahmed; The Biochemical Journal 1992, V286, P377 HCAPLUS
(2) Anon; WO 9321315 1993 HCAPLUS
(3) Anon; WO 9321316 1993 HCAPLUS
(4) Bard; US 5556753 1996 HCAPLUS
(5) Bergendahl; Neuroendocrinol 1992, V56, P913 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:272116 HCAPLUS
DOCUMENT NUMBER: 132:304925
TITLE: Constitutively active human G protein-coupled receptor mutants
INVENTOR(S): Behan, Dominic P.; Lehmann-Bruinsma, Karin; Chalmers, Derek T.; Chen, Ruoping; Dang, Huong T.; Gore, Martin; Liaw, Chen W.; Lin, I-Lin; Lowitz, Kevin; White, Carol
PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000022131	A2	20000420	WO 1999-US24065	19991013
WO 2000022131	A3	20010222		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9962991	A1	20000501	AU 1999-62991	19990112

PRIORITY APPLN. INFO.:

US 1998-170496	19981013
US 1998-108029	19981112
US 1998-109213	19981120
US 1998-110060	19981127
US 1999-120416	19990216
US 1999-121852	19990226
US 1999-123944	19990312
US 1999-123945	19990312
US 1999-123946	19990312
US 1999-123948	19990312
US 1999-123949	19990312
US 1999-123951	19990312
US 1999-136436	19990528
US 1999-136437	19990528
US 1999-136439	19990528
US 1999-137127	19990528
US 1999-137131	19990528
US 1999-137567	19990528
US 1999-141448	19990630
US 1999-151114	19990827

AB The invention relates to transmembrane receptors, more particularly to human G protein-coupled receptors for which the endogenous ligand is unknown ("orphan GPCR receptors"), and most particularly to mutated (non-endogenous) versions of the human GPCRs with constitutive activity. CDNA encoding these mutant receptors, plasmids contg. this cDNA, and host cells transformed with these plasmids are claimed. These mutant receptors could be used to screen for agonists, partial agonists, and reverse agonists which might be used as therapeutic agents. Thus, using an algorithmic approach, the 16th amino acid (located in the IC3 region of the receptor) from a conserved proline residue (located in the TM6 region of the receptor) was mutated, most preferably to a lysine residue. The constitutive activation of the resulting receptor mutant was demonstrated in a variety of ways, e.g., by adenyl cyclase assays.

IT **264867-18-7P**
RL: ARG (Analytical reagent use); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; constitutively active human G protein-coupled

receptor mutants)
IT **201099-18-5**, Melanocortin-4 receptor (human)
RL: PRP (Properties)
(unclaimed protein sequence; constitutively active human G protein-coupled receptor mutants)

L22 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:8118 HCAPLUS
DOCUMENT NUMBER: 130:61608
TITLE: Cells expressing mammalian melanocortin receptors for drug screening and transgenic animals with receptor gene knockout
INVENTOR(S): Cone, Roger D.; Chen, Wenbiao; Low, Malcolm J.
PATENT ASSIGNEE(S): Oregon Health Sciences University, USA
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856914	A1	19981217	WO 1998-US12098	19980612
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9879595	A1	19981230	AU 1998-79595	19980612
PRIORITY APPLN. INFO.:			US 1997-50063	19970613
			WO 1998-US12098	19980612

AB This invention provides methods and reagents for developing naturally-occurring and synthetic agonists and antagonists specific for a mammalian melanocortin receptor such as MC5-R. Also provided by the invention are nucleic acids, constructs, vectors and methods for producing an animal bearing a genetically-disrupted endogenous M5C-R melanocortin receptor, in both the heterozygous and homozygous condition. The cDNAs for mouse and human MC1-R, bovine and human MC2-R, rat MC3-R, human MC4-R and mouse MC5-R were cloned and expressed in mammalian cells, e.g., 293 or mouse Y1 cells, and the ligand binding characteristics were detd. MC5-R knockout mice were also prepd. and the consequences of this knockout were detd. Thus, MC5-R was found to regulate protein secretion by the lacrimal gland. MC5-R was also shown to be required for porphyrin prodn. in the Harderian gland.
IT **201099-18-5P**, Melanocortin-4 receptor (human)
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR (Biological process); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(amino acid sequence; cells expressing mammalian melanocortin receptors for drug screening and transgenic animals with receptor gene knockout)
REFERENCE COUNT: 9
REFERENCE(S):
(1) Chen, W; Cell 1997, V91(6), P789 HCAPLUS
(2) Huszar, D; Cell 1997, V88(1), P131 HCAPLUS
(3) Labbe, O; Biochemistry 1994, V33, P4543 HCAPLUS
(4) Millennium Pharmaceuticals Inc; WO 9747316 A 1997 HCAPLUS
(5) Mountjoy, K; Molecular Endocrinology 1994, V8(10),

P1298 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:176017 HCAPLUS
DOCUMENT NUMBER: 128:226679
TITLE: Methods and reagents for discovering and using mammalian melanocortin receptor agonists and antagonists to modulate feeding behavior in animals
INVENTOR(S): Cone, Roger D.; Fan, Wei; Boston, Bruce A.; Kesterton, Robert A.; Lu, Dongsi; Chen, Wenbiao
PATENT ASSIGNEE(S): Oregon Health Sciences University, USA; Cone, Roger D.; Fan, Wei; Boston, Bruce A.; Kesterton, Robert A.; Lu, Dongsi; Chen, Wenbiao
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810068	A2	19980312	WO 1997-US15565	19970904
WO 9810068	A3	19980625		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6100048	A	20000808	US 1996-706281	19960904
AU 9741812	A1	19980326	AU 1997-41812	19970904
AU 719954	B2	20000518		
EP 935655	A1	19990818	EP 1997-939799	19970904
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

US 1996-706281	19960904
US 1992-866560	19920410
US 1992-886979	19920521
US 1993-44812	19930408
US 1995-466906	19950606
US 1995-478992	19950607
WO 1997-US15565	19970904

OTHER SOURCE(S): MARPAT 128:226679

AB The present invention provides recombinant expression constructs comprising nucleic acid encoding mammalian melanocortin receptors, and mammalian cells into which said recombinant expression constructs have been introduced that express functional mammalian melanocortin receptors. Thus, cDNAs for 7 different melanocortin receptors were cloned from mammalian sources: mouse and human .alpha.-MSH receptors, human and bovine ACTH receptors, rat MC-3 receptor, human MC-4 receptor, and mouse MC-5 receptor. The invention provides a panel of transformed mammalian cells expressing melanocortin receptors for screening compds. for receptor

agonist and antagonist activity. The plasmid vector for the expression of the melanocortin receptors comprises the cAMP response element (CRE) linked to a reporter .beta.-galactosidase gene. The invention also provides methods for using such panels of melanocortin receptor-expressing mammalian cells to specifically detect and identify agonists and antagonists for each melanocortin receptor, as well as patterns of agonist and antagonist activity of said compds. for the class of melanocortin receptors. Such screening methods provide a means for identifying compds. with patterns of melanocortin agonist and antagonist activity which is assocd. with the capacity to influence or modify metab. and behavior, particularly feeding behavior.

IT **201099-18-5**, Melanocortin-4 receptor (human)
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; methods and reagents for discovering and using mammalian melanocortin receptor agonists and antagonists to modulate feeding behavior in animals)

L22 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:287164 HCAPLUS
DOCUMENT NUMBER: 126:302366
TITLE: Melanocortin receptor cDNA sequences, receptor characterization, gene mapping, recombinant expression, and application in gene therapy
INVENTOR(S): Yamada, Tadataka; Gantz, Ira
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA
SOURCE: U.S., 58 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5622860	A	19970422	US 1994-200711	19940217
US 5703220	A	19971230	US 1996-671525	19960627
US 5710265	A	19980120	US 1996-672109	19960627
US 6117975	A	20000912	US 1996-629335	19960723
US 5817787	A	19981006	US 1997-842045	19970423
US 5869257	A	19990209	US 1997-842238	19970423
PRIORITY APPLN. INFO.:			US 1994-200711	19940217
			US 1996-671525	19960627
			US 1996-672109	19960627

AB Genes encoding melanocortin receptors have been identified, isolated, cloned and localized to their chromosomal positions. These genes have been used to transfect mammalian cells lacking endogenous melanocortin receptors to induce expression. Addnl., melanocortin receptor binding, secondary signalling, and tissue distribution has been characterized. The genes and their gene products may therefore be used to to provide therapeutic vehicles for the treatment of processes involving the function of melanocortin receptors.

IT **151032-23-4P**
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)

(melanocortin receptor cDNA sequences, receptor characterization, gene mapping, recombinant expression, and application in gene therapy)

L22 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:641595 HCAPLUS
DOCUMENT NUMBER: 119:241595
TITLE: Molecular cloning, expression, and gene localization of a fourth melanocortin receptor
AUTHOR(S): Gantz, Ira; Miwa, Hiroto; Konda, Yoshitaka; Shimoto, Yoshimasa; Tashiro, Takao; Watson, Stanley J.; DelValle, John; Yamada, Tadataka
CORPORATE SOURCE: Med. Cent., Univ. Michigan, Ann Arbor, MI, 48109-0386, USA
SOURCE: J. Biol. Chem. (1993), 268(20), 15174-9
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The recent cloning of three melanocortin receptors suggests an unexpected diversity in this family of seven transmembrane G-protein linked receptors. Herein, the authors report the cloning, expression, and gene localization of a fourth human melanocortin receptor, the melanocortin-4 receptor. By Northern blot anal. and in situ hybridization, this receptor is expressed primarily in the brain, but its expression is notably absent in the adrenal cortex, melanocytes, and placenta. Agonist stimulation of COS-1 cells transiently transfected and L-cells permanently transfected with the coding region of the cloned melanocortin-4 receptor leads to increases in intracellular cyclic 3',5'-adenosine monophosphate. The profile of the responses of the melanocortin-4 receptor to different melanocortins distinguishes it from melanocortin receptors previously described. Using the technique of fluorescent in situ hybridization, the gene encoding the melanocortin-4 receptor was localized to chromosome 18 (q21.3).
IT **151032-23-4**
RL: BIOL (Biological study)
(amino acid sequence and expression in brain)

=> D l1 rn cn lc nte sql kwic can tot

L1 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2001 ACS
RN 264867-18-7 REGISTRY
CN G protein-coupled receptor MC4 [244-lysine] (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 135: PN: WO0022131 SEQID: 136 claimed protein
LC STN Files: CA, CAPLUS
SQL 332

SEQ 251 IGVFVVCWAP FFLHLIFYIS CPQNPYCVCF MSHFNLYLIL IMCNSIIDPL
========== ==========
301 IYALRSQELR KTFKEIICCY PLGGLCDLSS RY
====
HITS AT: 281-304

REFERENCE 1: 132:304925

```
L1   ANSWER 2 OF 8  REGISTRY  COPYRIGHT 2001 ACS
RN   260778-01-6  REGISTRY
CN   2: PN: WO0014115 FIGURE: 1 unclaimed protein (9CI)  (CA INDEX NAME)
LC   STN Files:   CA, CAPLUS, TOXLIT, USPATFULL
SQL  332

SEQ    251 IGVFVVCWAP FFLHLIFYIS CPQNPYCVCF MSHFNLYLIL IMCNSIIDPL
                                           ========== ==========
       301 IYALRSQELR KTFKEIICCY PLGGLCDLSS RY
           ====
HITS AT:   281-304

REFERENCE   1:  132:217147

L1   ANSWER 3 OF 8  REGISTRY  COPYRIGHT 2001 ACS
RN   258323-89-6  REGISTRY
CN   4: PN: WO0006777 FIGURE: 3 unclaimed protein (9CI)  (CA INDEX NAME)
LC   STN Files:   CA, CAPLUS, TOXLIT
SQL  290

SEQ    201 GAITLTILIG VFVVCWAPFF LHLIFYISCP QNPYCVCFMS HFNLYLILIM
                                                 == ==========
       251 CNSIIDPLIY ALRSQELRKT FKEIICCYPL GGLCDLSSRY
           ========== ==
HITS AT:   239-262

REFERENCE   1:  132:162049

L1   ANSWER 4 OF 8  REGISTRY  COPYRIGHT 2001 ACS
RN   258322-98-4  REGISTRY
CN   Melanocortin 4 pituitary hormone receptor (swine mutant 1) (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   5: PN: WO0006777 FIGURE: 3 claimed protein
LC   STN Files:   CA, CAPLUS, TOXLIT
SQL  248

SEQ    201 QNPYCVCFMS HFNLYLILIM CNSIIDPLIY ALRSQELRKT FKEIICCY
                  == ========== ========== ==
HITS AT:   209-232

REFERENCE   1:  132:162049

L1   ANSWER 5 OF 8  REGISTRY  COPYRIGHT 2001 ACS
RN   201099-18-5  REGISTRY
CN   Melanocortin-4 receptor (human) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   4: PN: US6100048 SEQID: 16 claimed protein
CN   74: PN: WO0022131 SEQID: 74 unclaimed protein
LC   STN Files:   BIOTECHNO, CA, CAPLUS, EMBASE, TOXLIT, USPATFULL
SQL  332

SEQ    251 IGVFVVCWAP FFLHLIFYIS CPQNPYCVCF MSHFNLYLIL IMCNSIIDPL
                                           ========== ==========
       301 IYALRSQELR KTFKEIICCY PLGGLCDLSS RY
           ====
```

HITS AT: 281-304

REFERENCE 1: 133:145447

REFERENCE 2: 132:304925

REFERENCE 3: 130:61608

REFERENCE 4: 128:226679

REFERENCE 5: 128:110853

L1 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2001 ACS
RN 201061-02-1 REGISTRY
CN Melanocortin-4 receptor [112-methionine] (human) (9CI) (CA INDEX NAME)
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
SQL 332

SEQ 251 IGVFVVCWAP FFLHLIFYIS CPQNPYCVCF MSHFNLYLIL IMCNSIIDPL
========== ==========
301 IYALRSQELR KTFKEIICCY PLGGLCDLSS RY
====
HITS AT: 281-304

REFERENCE 1: 128:110853

L1 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2001 ACS
RN 201060-99-3 REGISTRY
CN Melanocortin-4 receptor [137-threonine] (human) (9CI) (CA INDEX NAME)
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
SQL 332

SEQ 251 IGVFVVCWAP FFLHLIFYIS CPQNPYCVCF MSHFNLYLIL IMCNSIIDPL
========== ==========
301 IYALRSQELR KTFKEIICCY PLGGLCDLSS RY
====
HITS AT: 281-304

REFERENCE 1: 128:110853

L1 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2001 ACS
RN 151032-23-4 REGISTRY
CN Receptor, melanocortin 4 (human reduced) (9CI) (CA INDEX NAME)
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
SQL 332

SEQ 251 IGVFVVCWAP FFLHLIFYIS CPQNPYCVCF MSHFNLYLIL IMCNSIIDPL
========== ==========
301 IYALRSQELR KTFKEIICCY PLGGLCDLSS RY
====
HITS AT: 281-304

REFERENCE 1: 126:302366

REFERENCE 2: 119:241595